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# THE MATHEMATICAL WAY OF THINKING[1]

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BY the mathematical way of thinking I mean first that form of reasoning through which mathematics penetrates into the sciences of the external world—physics, chemistry, biology, economics, etc., and even into our everyday thoughts about human affairs, and secondly that form of reasoning which the mathematician, left to himself, applies in his own field. By the mental process of thinking we try to ascertain truth; it is our mind's effort to bring about its own enlightenment by evidence. Hence, just as truth itself and the experience of evidence, it is something fairly uniform and universal in character. Appealing to the light in our innermost self, it is neither reducible to a set of mechanically applicable rules, nor is it divided into watertight compartments like historic, philosophical, mathematical thinking, etc. We mathematicians are no Ku Klux Klan with a secret ritual of thinking. True, nearer the surface there are certain techniques and differences; for instance, the procedures of fact-finding in a courtroom and in a physical laboratory are conspicuously different. However, you should not expect me to describe the mathematical way of thinking much more clearly than one can describe, say, the democratic way of life.

A movement for the reform of the teaching of mathematics, which some decades ago made quite a stir in Germany under the leadership of the great mathematician Felix Klein, adopted the slogan "functional thinking." The important thing which the average educated man should have learned in his mathematics classes, so the reformers claimed, is thinking in terms of *variables and functions.* A function de-

[1] Address delivered at the Bicentennial Celebration Conference of the University of Pennsylvania, September 17, 1940.

scribes how one variable $y$ depends on another $x$; or more generally, it maps one variety, the range of a variable element $x$, upon another (or the same) variety. This idea of function or mapping is certainly one of the most fundamental concepts, which accompanies mathematics at every step in theory and application.

Our federal income tax law defines the tax $y$ to be paid in terms of the income $x$; it does so in a clumsy enough way by pasting several linear functions together, each valid in another interval or bracket of income. An archeologist who, five thousand years from now, shall unearth some of our income tax returns together with relics of engineering works and mathematical books, will probably date them a couple of centuries earlier, certainly before Galileo and Vieta. Vieta was instrumental in introducing a consistent algebraic symbolism; Galileo discovered the quadratic law of falling bodies, according to which the drop $s$ of a body falling in a vacuum is a quadratic function of the time $t$ elapsed since its release:

$$s = \tfrac{1}{2}gt^2, \qquad (1)$$

$g$ being a constant which has the same value for each body at a given place. By this formula Galileo converted a natural law inherent in the actual motion of bodies into an *a priori* constructed mathematical function, and that is what physics endeavors to accomplish for every phenomenon. The law is of much better design than our tax laws. It has been designed by Nature, who seems to lay her plans with a fine sense for mathematical simplicity and harmony. But then Nature is not, as our income and excess profits tax laws are, hemmed in by having to be comprehensible to our legislators and chambers of commerce.

Right from the beginning we encounter these characteristic features of the mathematical process: 1) variables, like $t$ and $s$ in the formula (1), whose possible values belong to a range, here the range of real numbers, which we can completely survey because it springs from our own free construction, 2) representation of these variables by symbols, and 3) functions or *a priori* constructed mappings of the range of one variable $t$ upon the range of another $s$. *Time* is the independent variable *kat exochen*.

In studying a function one should let the independent variable run over its full range. A conjecture about the mutual interdependence of quantities in nature, even before it is checked by experience, may be probed in thought by examining whether it carries through over the whole range of the independent variables. Sometimes certain simple *limiting cases* at once reveal that the conjecture is untenable. Leibnitz taught us by his *principle of continuity* to consider rest not as contradictorily opposed to motion, but as a limiting case of motion. Arguing by continuity he was able *a priori* to refute the laws of impact proposed by Descartes. Ernst Mach gives this prescription: "After having reached an opinion for a special case, one gradually modifies the circumstances of this case as far as possible, and in so doing tries to stick to the original opinion as closely as one can. There is no procedure which leads more safely and with greater mental economy to the simplest interpretation of all natural events." Most of the variables with which we deal in the analysis of nature are continuous variables like time, but although the word seems to suggest it, the mathematical concept is not restricted to this case. The most important example of a discrete variable is given by the sequence of natural numbers or integers 1, 2, 3, . . . Thus the number of divisors of an arbitrary integer $n$ is a function of $n$.

In Aristotle's logic one passes from the individual to the general by exhibiting certain abstract features in a given object and discarding the remainder, so that two objects fall under the same concept or belong to the same genus if they have those features in common. This descriptive classification, *e.g.*, the description of plants and animals in botany and zoology, is concerned with the actual existing objects. One might say that Aristotle thinks in terms of substance and accident, while the functional idea reigns over the formation of mathematical concepts. Take the notion of ellipse. Any ellipse in the $x$-$y$-plane is a set $E$ of points $(x, y)$ defined by a quadratic equation

$$ax^2 + 2bxy + cy^2 = 1$$

whose coefficients $a, b, c$ satisfy the conditions

$$a > 0, \quad c > 0, \quad ac - b^2 > 0.$$

The set $E$ depends on the coefficients $a, b, c$; we have a function $E(a, b, c)$ which gives rise to an individual ellipse by assigning definite values to the variable coefficients $a, b, c$. In passing from the individual ellipse to the general notion one does not discard any specific difference, one rather makes certain characteristics (here represented by the coefficients) variable over an *a priori* surveyable range (here described by the inequalities). The notion thus extends over all *possible*, rather than over all *actually existing*, specifications.[1]

From these preliminary remarks about functional thinking I now turn to a more systematic argument. Mathematics is notorious for the thin air of abstraction in which it moves. This bad reputation is only half deserved. Indeed, the first difficulty the man in the street encounters when he is taught to think mathematically is that he must learn to look things much more squarely in the face; his belief in words must be shattered; he must learn to think more concretely.

[1] Compare about this contrast Ernst Cassirer, "Substanzbegriff und Funktionsbegriff," 1910, and my critical remark, "Philosophie der Mathematik und Naturwissenschaft," 1923, p. 111.

Only then will he be able to carry out the second step, the step of abstraction where intuitive ideas are replaced by purely symbolic construction.

About a month ago I hiked around Longs Peak in the Rocky Mountain National Park with a boy of twelve, Pete. Looking up at Longs Peak he told me that they had corrected its elevation and that it is now 14,255 feet instead of 14,254 feet last year. I stopped a moment asking myself what this could mean to the boy, and should I try to enlighten him by some Socratic questioning. But I spared Pete the torture, and the comment then withheld, will now be served to you. Elevation is elevation above sea level. But there is no sea under Longs Peak. Well, in idea one continues the actual sea level under the solid continents. But how does one construct this ideal closed surface, the geoid, which coincides with the surface of the oceans over part of the globe? If the surface of the ocean were strictly spherical, the answer would be clear. However, nothing of this sort is the case. At this point dynamics comes to our rescue. Dynamically the sea level is a surface of constant potential $\phi = \phi_0$; more exactly $\phi$ denotes the gravitational potential of the earth, and hence the difference of $\phi$ at two points $P, P'$ is the work one must put into a small body of mass 1 to transfer it from $P$ to $P'$. Thus it is most reasonable to define the geoid by the dynamical equation $\phi = \phi_0$. If this constant value of $\phi$ fixes the elevation zero, it is only natural to define any fixed altitude by a corresponding constant value of $\phi$, so that a peak $P$ is called higher than $P'$ if one gains energy by flying from $P$ to $P'$. The geometric concept of altitude is replaced by the dynamic concept of potentional or energy. Even for Pete, the mountain climber, this aspect is perhaps the most important: the higher the peak the greater—*ceteris paribus*—the mechanical effort in climbing it. By closer scrutiny one finds that in almost every respect the potential is the relevant factor. For instance the barometric measurement of altitude is based on the fact that in an atmosphere of given constant temperature the potential is proportional to the logarithm of the atmospheric pressure, whatever the nature of the gravitational field. Thus atmospheric pressure, generally speaking, indicates potential and not altitude. Nobody who has learned that the earth is round and the vertical direction is not an intrinsic geometric property of space but the direction of gravity should be surprised that he is forced to discard the geometric idea of altitude in favor of the dynamic more concrete idea of potential. Of course there is a relationship to geometry: In a region of space so small that one can consider the force of gravity as constant throughout this region, we have a fixed vertical direction, and potential differences are proportional to differences of altitude measured in that direction. Altitude, height, is a word which has a clear meaning when I ask how high the ceiling of this room is above its floor. The meaning gradually loses precision when we apply it to the relative altitudes of mountains in a wider and wider region. It dangles in the air when we extend it to the whole globe, unless we support it by the dynamical concept of potential. Potential is more concrete than altitude because it is generated by and dependent on the mass distribution of the earth.

Words are dangerous tools. Created for our everyday life they may have their good meanings under familiar limited circumstances, but Pete and the man in the street are inclined to extend them to wider spheres without bothering about whether they then still have a sure foothold in reality. We are witnesses of the disastrous effects of this witchcraft of words in the political sphere where all words have a much vaguer meaning and human passion so often drowns the voice of reason. The scientist must thrust through the fog of abstract words to reach the concrete rock of reality. It seems to me that the science of economics has a particularly hard job, and will still have to spend much effort, to live up to this principle. It is, or should be, common to all sciences, but physicists and mathematicians have been forced to apply it to the most fundamental concepts where the dogmatic resistance is strongest, and thus it has become their second nature. For instance, the first step in explaining relativity theory must always consist in shattering the dogmatic belief in the temporal terms past, present, future. You can not apply mathematics as long as words still becloud reality.

I return to relativity as an illustration of this first important step preparatory to mathematical analysis, the step guided by the maxim, "Think concretely." As the root of the words *past, present, future,* referring to time, we find something much more tangible than time, namely, the causal structure of the universe. Events are localized in space and time; an event of small extension takes place at a space-time or world point, a here-now. After restricting ourselves to events on a plane $E$ we can depict the events by a graphic timetable in a three-dimensional diagram with a horizontal $E$ plane and a vertical $t$ axis on which time $t$ is plotted. A world point is represented by a point in this picture, the motion of a small body by a world line, the propagation of light with its velocity $c$ radiating from a light signal at the world point $O$ by a vertical straight circular cone with vertex at $O$ (light cone). The *active future* of a given world point $O$, here-now, contains all those events which can still be influenced by what happens at $O$, while its *passive past* consists of all those world points from which any influence, any message, can reach $O$. I

here-now can no longer change anything that lies outside the active future; all events of which I here-now can have knowledge by direct observation or any records thereof necessarily lie in the passive past. We interpret the words past and future in this causal sense where they express something very real and important, the causal structure of the world.

The new discovery at the basis of the theory of relativity is the fact that no effect may travel faster than light. Hence while we formerly believed that active future and passive past bordered on each other along the cross-section of *present,* the horizontal plane $t = \text{const.}$ going through $O$, Einstein taught us that the active future is bounded by the forward light cone and the passive past by its backward continuation. Active

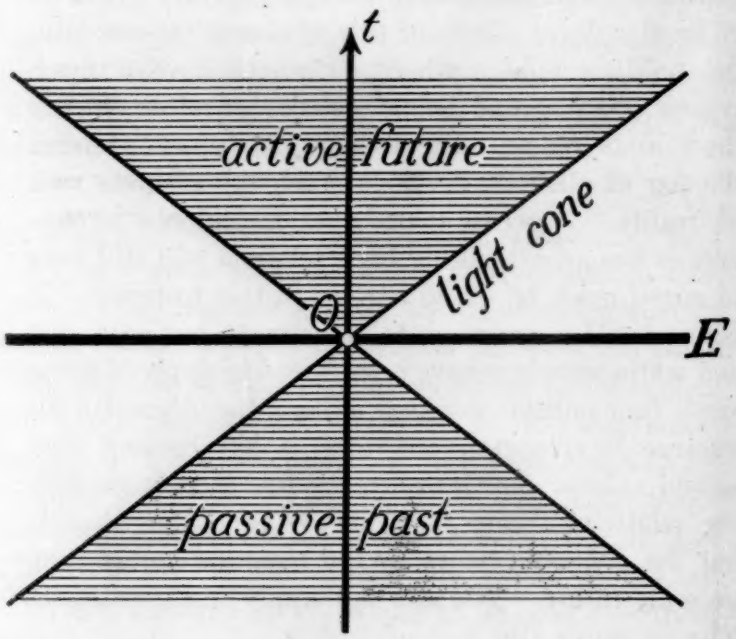


FIG. 1

future and passive past are separated by the part of the world lying between these cones, and with this part I am here-now not at all causally connected. The essential positive content of relativity theory is this new insight into the causal structure of the universe. By discussing the various interpretations of such a simple question as whether two men, say Bill on earth and Bob on Sirius, are contemporaries, as to whether it means that Bill can send a message to Bob, or Bob a message to Bill, or even that Bill can communicate with Bob by sending a message and receiving an answer, etc., I often succeed soon in accustoming my listener to thinking in terms of causal rather than his wonted temporal structure. But when I tell him that the causal structure is not a stratification by horizontal layers $t = \text{const.}$, but that active future and passive past are of cone-like shape with an interstice between, then some will discern dimly what I am driving at, but every honest listener will say: Now you draw a figure, you speak in pictures; how far does the simile go, and what is the naked truth to be conveyed by it?

Our popular writers and news reporters, when they have to deal with physics, indulge in similes of all sorts; the trouble is that they leave the reader helpless in finding out how far these pungent analogies cover the real issue, and therefore more often lead him astray than enlighten him. In our case one has to admit that our diagram is no more than a picture, from which, however, the real thing emerges as soon as we replace the intuitive space in which our diagrams are drawn by its construction in terms of sheer symbols. Then the phrase that the world is a four-dimensional continuum changes from a figurative form of speech into a statement of what is literally true. At this second step the mathematician turns abstract, and here is the point where the layman's understanding most frequently breaks off: the intuitive picture must be exchanged for a symbolic construction. "By its geometric and later by its purely symbolic construction," says Andreas Speiser, "mathematics shook off the fetters of language, and one who knows the enormous work put into this process and its ever recurrent surprising successes can not help feeling that mathematics to-day is more efficient in its sphere of the intellectual world, than the modern languages in their deplorable state or even music are on their respective fronts." I shall spend most of my time to-day in an attempt to give you an idea of what this magic of symbolic construction is.

To that end I must begin with the simplest, and in a certain sense most profound, example: the natural numbers or *integers* by which we *count* objects. The symbols we use here are strokes put one after another. The objects may disperse, "melt, thaw and resolve themselves into a dew," but we keep this record of their number. What is more, we can by a constructive process decide for two numbers represented through such symbols which one is the larger, namely by checking one against the other, stroke by stroke. This process reveals differences not manifest in direct observation, which in most instances is incapable of distinguishing between even such low numbers as 21 and 22. We are so familiar with these miracles which the number symbols perform that we no longer wonder at them. But this is only the prelude to the mathematical step proper. We do not leave it to chance which numbers we shall meet by counting actual objects, but we generate the open sequence of *all possible* numbers which starts with 1 (or 0) and proceeds by adding to any number symbol $n$ already reached one more stroke, whereby it changes into the following number $n'$. As I have often said before, being is thus projected onto the background of the possible, or more precisely onto a manifold of possibilities which unfolds by iteration and is open into infinity. Whatever number $n$ we are given, we always deem it possible to pass

to the next $n'$. "Number goes on." This intuition of the "ever one more," of the open countable infinity, is basic for all mathematics. It gives birth to the simplest example of what I termed above an *a priori* surveyable range of variability. According to this process by which the integers are created, functions of an argument ranging over all integers $n$ are to be defined by so-called complete induction, and statements holding for all $n$ are to be proved in the same fashion. The principle of this inference by complete induction is as follows. In order to show that every number $n$ has a certain property $V$ it is sufficient to make sure of two things:

1) 0 has this property;

2) If $n$ is any number which has the property $V$, then the next number $n'$ has the property $V$.

It is practically impossible, and would be useless, to write out in strokes the symbol of the number $10^{12}$, which the Europeans call a billion and we in this country, a thousand billions. Nevertheless we talk about spending more than $10^{12}$ cents for our defense program, and the astronomers are still ahead of the financiers. In July the *New Yorker* carried this cartoon: man and wife reading the newspaper over their breakfast and she looking up in puzzled despair: "Andrew, how much *is* seven hundred billion dollars?" A profound and serious question, lady! I wish to point out that only by passing through the *infinite* can we attribute any significance to such figures. 12 is an abbreviation of

$$10^{12} = \underbrace{10 \cdot 10 \cdot 10 \cdot 10 \cdot 10 \cdot 10 \cdot 10 \cdot 10 \cdot 10 \cdot 10 \cdot 10 \cdot 10}_{/\ /\ /\ /\ /\ /\ /\ /\ /\ /\ /\ /.}$$

can not be understood without defining the function $10 \cdot n$ for *all* $n$, and this is done through the following definition by complete induction:

$$10 \cdot 0 = 0,$$
$$10 \cdot n' = (10 \cdot n)''''''''''.$$

The dashes constitute the explicit symbol for 10, and, as previously, each dash indicates transition to the next number. Indian, in particular Buddhist, literature indulges in the possibilities of fixing stupendous numbers by the decimal system of numeration which the Indians invented, *i.e.*, by a combination of sums, products and powers. I mention also Archimedes's treatise "On the counting of sand," and Professor Kasner's Googolplex in his recent popular book on "Mathematics and the Imagination."

Our conception of *space* is, in a fashion similar to that of natural numbers, depending on a constructive grip on all *possible* places. Let us consider a metallic disk in a plane $E$. Places on the disk can be marked *in concreto* by scratching little crosses on the plate. But relatively to two axes of coordinates and a standard length scratched into the plate we can also put ideal marks in the plane outside the disk by giving the numerical values of their two coordinates. Each coordinate varies over the *a priori* constructed range of real numbers. In this way astronomy uses our solid earth as a base for plumbing the sidereal spaces. What a marvelous feat of imagination when the Greeks first constructed the shadows which earth and moon, illumined by the sun, cast in empty space and thus explained the eclipses of sun and moon! In analyzing a continuum, like space, we shall here proceed in a somewhat more general manner than by measurement of coordinates and adopt the *topological* viewpoint, so that two continua arising one from the other by continuous deformation are the same to us. Thus the following exposition is at the same time a brief introduction to an important branch of mathematics, topology.

The symbols for the localization of points on the one-dimensional continuum of a straight line are the *real numbers*. I prefer to consider a *closed* one-dimensional continuum, the circle. The most fundamental statement about a continuum is that it may be divided into parts. We catch all the points of a continuum by spanning a net of division over it, which we refine by repetition of a definite process of subdivision *ad infinitum*. Let $S$ be any division of the circle into a number of arcs, say $l$ arcs. From $S$ we derive a new division $S'$ by the process of *normal subdivision*, which consists in breaking each arc into two. The number of arcs in $S'$ will then be $2l$. Running around the circle in a definite sense (orientation) we may distinguish the two pieces, in the order in which we meet them, by the marks 0 and 1; more explicitly, if the arc is denoted by a symbol $\alpha$ then these two pieces are designated as $\alpha 0$ and $\alpha 1$. We start with the division $S_0$ of the circle into two arcs + and −; either is topologically a cell, *i.e.*, equivalent to a segment. We then iterate the process of normal subdivision and thus obtain $S_0'$, $S_0''$, $\cdots$, seeing to it that the refinement of the division ultimately pulverizes the whole circle. If we had not renounced the use of metric properties we could decree that the normal subdivision takes place by cutting each arc into two *equal* halves. We introduce no such fixation; hence the actual performance of the process involves a wide measure of arbitrariness. However, the *combinatorial scheme* according to which the parts reached at any step border on each other, and according to which the division progresses, is unique and perfectly fixed. Mathematics cares for this symbolic scheme only. By our notation the parts occurring at the consecutive divisions are *catalogued* by symbols of this type

$$+.011010001$$

with + or − before the dot and all following places occupied by either 0 or 1. We see that we arrive at the familiar symbols of binary (not decimal) fractions. A point is caught by an infinite sequence of arcs of the consecutive divisions such that each arc arises from the preceding one by choosing one of the two pieces

into which it breaks by the next normal subdivision, and the point is thus fixed by an infinite binary fraction.

Let us try to do something similar for two-dimensional continua, *e.g.*, for the surface of a sphere or a

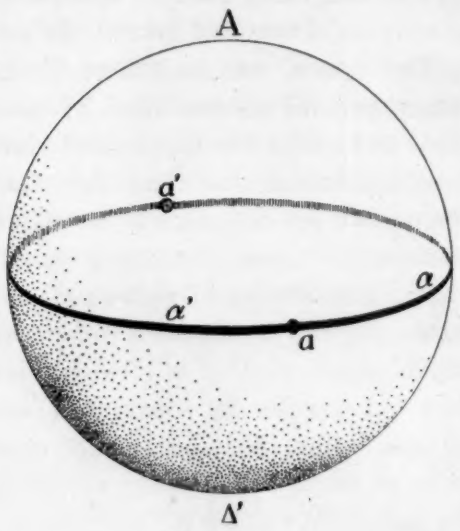


FIG. 2

torus. The figures show how we may cast a very coarse net over either of them, the one consisting of two, the other of four meshes; the globe is divided into its upper and lower halves by the equator, the torus is welded together from four rectangular plates. The meshes are two-dimensional cells, or briefly, 2-cells which are topologically equivalent to a circular disk. The combinatorial description is facilitated by introducing also the vertices and edges of the division, which

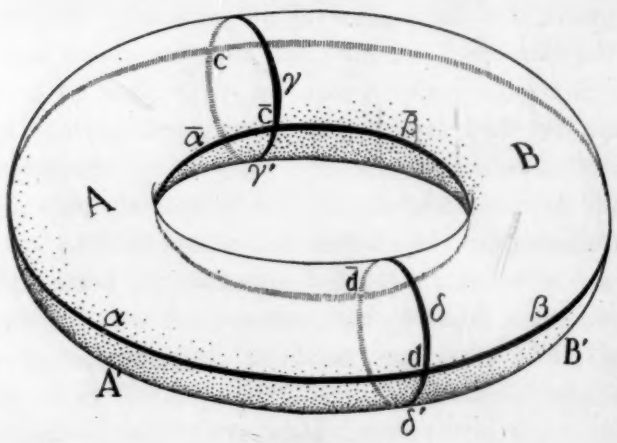


FIG. 3

are 0- and 1-cells. We attach arbitrary symbols to them and state in symbols for each 2-cell which 1-cells bound it, and for each 1-cell by which 0-cells it is bounded. We then arrive at a *topological scheme* $S_0$. Here are our two examples:

*Sphere.* $A \to \alpha, \alpha'$. $A' \to \alpha, \alpha'$. $\alpha \to a, a'$. $\alpha' \to a, a'$.
($\to$ means: bound by)

*Torus.* $A \to \alpha, \bar{\alpha}, \gamma, \delta$. $A' \to \alpha, \bar{\alpha}, \gamma', \delta'$.
$B \to \beta, \bar{\beta}, \gamma, \delta$. $B' \to \beta, \bar{\beta}, \gamma', \delta'$.
$\alpha \to c, d$. $\bar{\alpha} \to \bar{c}, \bar{d}$. $\beta \to c, d$. $\bar{\beta} \to \bar{c}, \bar{d}$.
$\gamma \to c, \bar{c}$. $\gamma' \to c, \bar{c}$. $\delta \to d, \bar{d}$. $\delta' \to d, \bar{d}$.

From this initial stage we proceed by iteration of a universal process of normal subdivision: On each 1-cell $\alpha = ab$ we choose a point which serves as a new vertex $\alpha$ and divides the 1-cell into two segments $\alpha a$ and $\alpha b$; in each 2-cell $A$ we choose a point $A$ and cut the cell into triangles by joining the newly created vertex $A$ with the old and new vertices on its bounding 1-cells by lines within the 2-cell. Just as in elementary geometry we denote the triangles and their sides by means of their vertices. The figure shows a pentagon before and after subdivision; the triangle $A\beta c$ is bounded by the 1-cells $\beta c$, $A\beta$, $Ac$, the 1-cell $Ac$ for instance by the vertices $c$ and $A$. We arrive at the following general purely symbolic description of the process by which the subdivided scheme $S'$ is derived from a given topological scheme $S$. Any symbol $e_2\ e_1\ e_0$ made up by the symbols of a 2-cell $e_2$, a 1-cell $e_1$ and a 0-cell $e_0$ in $S$ such that $e_2$ is bounded by $e_1$ and $e_1$ bounded by $e_0$ represents a 2-cell $e'_2$ of $S'$. This 2-cell $e'_2 = e_2 e_1 e_0$ in $S'$ is part of the 2-cell $e_2$ in $S$. The symbols of cells in $S'$ which bound a given cell are derived from its symbol by dropping any one of its constituent letters. Through iteration of this symbolic process the initial scheme $S_0$ gives rise to a sequence of derived schemes $S_0'$, $S_0''$, $S_0'''$, $\cdots$. What we have done is nothing else than devise a systematic cataloguing of the parts created by consecutive subdivisions. A *point* of our continuum is caught by a sequence

$$e\ e'\ e'' \cdots \qquad (2)$$

which starts with a 2-cell $e$ of $S_0$ and in which the 2-cell $e^{(n)}$ of the scheme $S^{(n)}$ is followed by one of the 2-cells $e^{(n+1)}$ of $S^{(n+1)}$ into which $e^{(n)}$ breaks up by our subdivision. (To do full justice to the inseparability of parts in a continuum this description ought to be slightly altered. But for the present purposes our simplified description will do.) We are convinced that not only may each point be caught by such a sequence (Eudoxos), but that an arbitrarily constructed sequence of this sort always catches a point (Dedekind, Cantor). The fundamental concepts of *limit, convergence* and *continuity* follow in the wake of this construction.

We now come to the decisive step of mathematical abstraction: we forget about what the symbols stand for. The mathematician is concerned with the catalogue alone; he is like the man in the catalogue room who does not care what books or pieces of an intuitively given manifold the symbols of his catalogue denote. He need not be idle; there are many operations which he may carry out with these symbols, without ever having to look at the things they stand for. Thus, replacing the points by their symbols (2) he turns the given manifold into a *symbolic construct* which we shall call the *topological space* $\{S_0\}$ because it is based on the scheme $S_0$ alone.

The details are not important; what matters is that once the initial finite symbolic scheme $S_0$ is given we are carried along by an absolutely rigid symbolic construction which leads from $S_0$ to $S_0'$, from $S_0'$ to $S_0''$, etc. The idea of iteration, first encountered with the natural numbers, again plays a decisive role. The realization of the symbolic scheme for a given manifold, say a sphere or a torus, as a scheme of consecutive divisions involves a wide margin of arbitrariness restricted only by the requirement that the pattern of the meshes ultimately becomes infinitely fine everywhere. About this point and the closely affiliated requirement that each 2-cell has the topological structure of a circular disk, I must remain a bit vague. However, the mathematician is not concerned with applying the scheme or catalogue to a given manifold, but only with the scheme itself, which contains no haziness whatsoever. And we shall presently see that even the physicist need not care greatly about that application. It was merely for heuristic purposes that we had to go the way from manifold through division to pure symbolism.

In the same purely symbolic way we can evidently construct not only 1- and 2- but also 3, 4, 5, . . . -dimensional manifolds. An $n$-dimensional scheme $S_0$ consists of symbols distinguished as 0, 1, 2, . . . , $n$-cells and associates with each $i$-cell $e_i$ $(i=1, 2, \cdot\cdot, n)$ certain $(i-1)$-cells of which one says that they bound $e_i$. It is clear how the process of normal subdivision carries over. *A certain such 4-dimensional scheme can be used for the localization of events,* of all possible here-nows; physical quantities which vary in space and time are functions of a variable point ranging over the corresponding symbolically constructed 4-dimensional topological space. In this sense the world *is* a 4-dimensional continuum. The causal structure, of which we talked before, will have to be constructed within the medium of this 4-dimensional world, *i.e.,* out of the symbolic material constituting our topological space. Incidentally the topological viewpoint has been adopted on purpose, because only thus our frame becomes wide enough to embrace both special and general relativity theory. The special theory envisages the causal structure as something geometrical, rigid, given once for all, while in the general theory it becomes flexible and dependent on matter in the same way as, for instance, the electromagnetic field.

In our analysis of nature we reduce the phenomena to simple elements each of which varies over a certain range of possibilities which we can survey *a priori* because we construct these possibilities *a priori* in a purely combinatorial fashion from some purely symbolic material. The manifold of space-time points is one, perhaps the most basic one, of these constructive elements of nature. We dissolve light into plane polarized monochromatic light beams with few variable characteristics like wave length which varies over the symbolically constructed continuum of real numbers. Because of this *a priori* construction we speak of a *quantitative* analysis of nature; I believe the word quantitative, if one can give it a meaning at all, ought to be interpreted in this wide sense. The power of science, as witnessed by the development of modern technology, rests upon the combination of *a priori* symbolic construction with systematic experience in the form of planned and reproducible reactions and their measurements. As material for the *a priori* construction, Galileo and Newton used certain features of reality like space and time which they considered as objective, in opposition to the subjective sense qualities, which they discarded. Hence the important role which geometric figures played in their physics. You probably know Galileo's words in the *Saggiatore* where he says that no one can read the great book of nature "unless he has mastered the code in which it is composed, that is, the mathematical figures and the necessary relations between them." Later we have learned that none of these features of our immediate observation, not even space and time, have a right to survive in a pretended truly objective world, and thus have

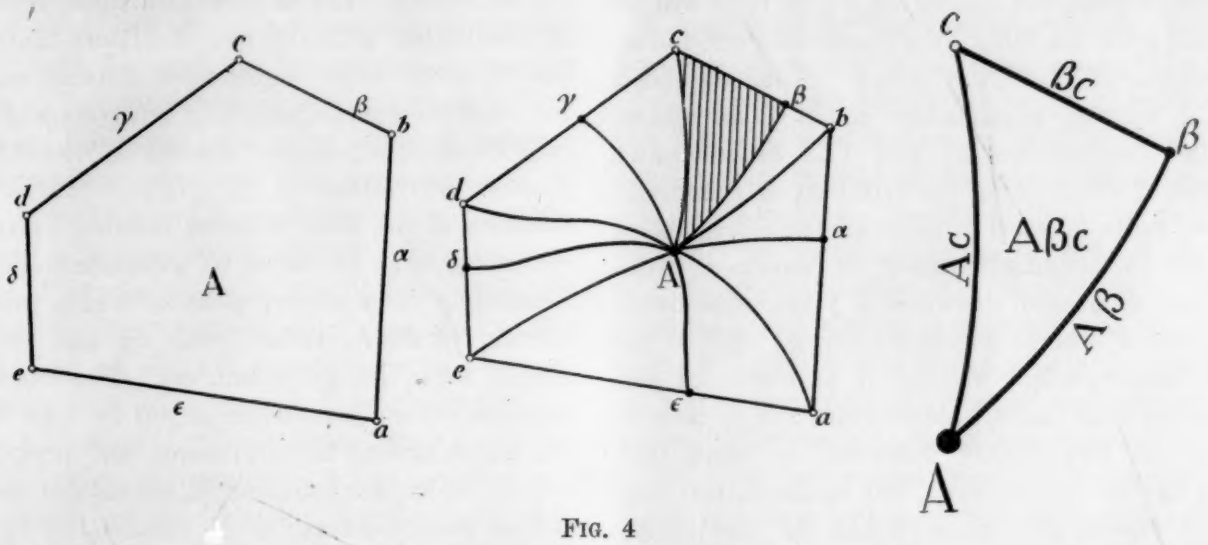


FIG. 4

gradually and ultimately come to adopt a purely symbolic combinatorial construction.

While a set of objects determines its number unambiguously, we have observed that a scheme of division $S_0$ with its consecutive derivatives $S_0'$, $S_0''$, $\cdots$ can be established on a given manifold in many ways involving a wide margin of arbitrariness. But the question whether two schemes,

$$S_0, S_0', S_0'' \cdots \text{ and } T_0, T_0', T_0'' \cdots$$

are fit to describe the same manifold is decidable in a purely mathematical way: it is necessary and sufficient that the two topological spaces $\{S_0\}$ and $\{T_0\}$ can be mapped one upon the other by a continuous one-to-one transformation—a condition which ultimately boils down to a certain relationship called isomorphism between the two schemes $S_0$ and $T_0$. (Incidentally the problem of establishing the criterion of isomorphism for two finite schemes in finite combinatorial form is one of the outstanding unsolved mathematical problems.) The connection between a given continuum and its symbolic scheme inevitably carries with it this notion of *isomorphism;* without it and without our understanding that isomorphic schemes are to be considered as not intrinsically different, no more than congruent figures in geometry, the mathematical concept of a topological space would be incomplete. Moreover it will be necessary to formulate precisely the conditions which every topological scheme is required to satisfy. For instance, one such condition demands that each 1-cell be bounded by exactly *two* 0-cells.

I can now say a little more clearly why the physicist is almost as disinterested as the mathematician in the particular way how a certain combinatorial scheme of consecutive divisions is applied to the continuum of here-nows which we called the world. Of course, somehow our theoretical constructions must be put in contact with the observable facts. The historic development of our theories proceeds by heuristic arguments over a long and devious road and in many steps from experience to construction. But systematic exposition should go the other way: first develop the theoretical scheme without attempting to define individually by appropriate measurements the symbols occurring in it as space-time coordinates, electromagnetic field strengths, etc., then describe, as it were in one breath, the contact of the whole system with observable facts. The simplest example I can find is the observed angle between two stars. The symbolic construct in the medium of the 4-dimensional world from which theory determines and predicts the value of this angle includes: (1) the world-lines of the two stars, (2) the causal structure of the universe, (3) the world position of the observer and the direction of his world line at the moment of observation. But a continuous deformation, a one-to-one continuous transformation of this whole picture, does not affect the value of the angle. *Isomorphic pictures lead to the same results concerning observable facts.* This is, in its most general form, the *principle of relativity.* The arbitrariness involved in our ascent from the given manifold to the construct is expressed by this principle for the opposite descending procedure, which the systematic exposition should follow.

So far we have endeavored to describe how a mathematical construct is distilled from the given raw material of reality. Let us now look upon these products of distillation with the eye of a pure mathematician. One of them is the sequence of natural numbers and the other the general notion of a topological space $\{S_0\}$ into which a topological scheme $S_0$ develops by consecutive derivations $S_0, S_0', S_0'', \cdots$. In both cases *iteration* is the most decisive feature. Hence all our reasoning must be based on evidence concerning that completely transparent process which generates the natural numbers, rather than on any principles of formal logic like syllogism, etc. The business of the constructive mathematician is *not* to draw logical conclusions. Indeed his arguments and propositions are merely an accompaniment of his actions, his carrying out of constructions. For instance, we run over the sequence of integers 0, 1, 2, . . . by saying alternatingly even, odd, even, odd, etc., and in view of the possibility of this inductive construction which we can extend as far as we ever wish, we formulate the general arithmetical proposition: "Every integer is even or odd." Besides the idea of iteration (or the sequence of integers) we make constant use of mappings or of the functional idea. For instance, just now we have defined a function $\pi(n)$, called parity, with $n$ ranging over all integers and $\pi$ capable of the two values 0 (even) and 1 (odd), by this induction:

$$\pi(0) = 0;$$
$$\pi(n') = 1 \text{ if } \pi(n) = 0, \qquad \pi(n') = 0 \text{ if } \pi(n) = 1.$$

Structures such as the topological schemes are to be studied in the light of the idea of *isomorphism.* For instance, when it comes to introducing operators $\tau$ which carry any topological scheme $S$ into a topological scheme $\tau(S)$ one should pay attention only to such operators or functions $\tau$ for which isomorphism of $S$ and $R$ entails isomorphism for $\tau(S)$ and $\tau(R)$.

Up to now I have emphasized the constructive character of mathematics. In our actual mathematics there vies with it the non-constructive *axiomatic method.* Euclid's axioms of geometry are the classical prototype. Archimedes employs the method with great acumen and so do later Galileo and Huyghens in erecting the science of mechanics. One defines all concepts in terms of a few undefined basic concepts and deduces all propositions from a number of basic

propositions, the axioms, concerning the basic concepts. In earlier times authors were inclined to claim *a priori* evidence for their axioms; however this is an epistemological aspect which does not interest the mathematician. Deduction takes place according to the principles of formal logic, in particular it follows the syllogistic scheme. Such a treatment *more geometrico* was for a long time considered the ideal of every science. Spinoza tried to apply it to ethics. For the mathematician the meaning of the words representing the basic concepts is irrelevant; any interpretation of them which fits, *i.e.*, under which the axioms become true, will be good, and all the propositions of the discipline will hold for such an interpretation because they are all logical consequences of the axioms. Thus $n$-dimensional Euclidean geometry permits another interpretation where points are distributions of electric current in a given circuit consisting of $n$ branches which connect at certain branch points. For instance, the problem of determining that distribution which results from given electromotoric forces inserted in the various branches of the net corresponds to the geometric construction of orthogonal projection of a point upon a linear subspace. From this standpoint mathematics treats of relations in a hypothetical-deductive manner without binding itself to any particular material interpretation. It is not concerned with the *truth* of axioms, but only with their *consistency;* indeed inconsistency would *a priori* preclude the possibility of our ever coming across a fitting interpretation. "Mathematics is the science which draws necessary conclusions," says B. Peirce in 1870, a definition which was in vogue for decades after. To me it seems that it renders very scanty information about the real nature of mathematics, and you are at present watching my struggle to give a fuller characterization. Past writers on the philosophy of mathematics have so persistently discussed the axiomatic method that I don't think it necessary for me to dwell on it at any greater length, although my exposition thereby becomes somewhat lopsided.

However I should like to point out that since the axiomatic attitude has ceased to be the pet subject of the methodologists its influence has spread from the roots to all branches of the mathematical tree. We have seen before that topology is to be based on a full enumeration of the axioms which a *topological scheme* has to satisfy. One of the simplest and most basic axiomatic concepts which penetrates all fields of mathematics is that of *group.* Algebra with its *"fields," "rings,"* etc., is to-day from bottom to top permeated by the axiomatic spirit. Our portrait of mathematics would look a lot less hazy, if time permitted me to explain these mighty words which I have just uttered, group, field and ring. I shall not try it, as little as I have stated the axioms characteristic for a topological scheme. But such notions and their kin have brought it about that modern mathematical research often is a dexterous blending of the constructive and the axiomatic procedures. Perhaps one should be content to note their mutual interlocking. But temptation is great to adopt one of these two views as the genuine primordial way of mathematical thinking, to which the other merely plays a subservient role, and it is possible indeed to carry this standpoint through consistently whether one decides in favor of construction or axiom.

Let us consider the first alternative. Mathematics then consists primarily of construction. The occurring sets of axioms merely *fix the range of variables entering into the construction.* I shall explain this statement a little further by our examples of causal structure and topology. According to the special theory of relativity the causal structure is once for all fixed and can therefore be explicitly constructed. Nay, it is reasonable to construct it together with the topological medium itself, as for instance a circle together with its metric structure is obtained by carrying out the normal subdivision by cutting each arc into two *equal* halves. In the general theory of relativity, however, the causal structure is something flexible; it has only to satisfy certain axioms derived from experience which allow a considerable measure of free play. But the theory goes on by establishing laws of nature which connect the flexible causal structure with other flexible physical entities, distribution of masses, electromagnetic field, etc., and these laws in which the flexible things figure as variables are in their turn *constructed* by the theory in an explicit *a priori* way. Relativistic cosmology asks for the topological structure of the universe as a whole, whether it is open or closed, etc. Of course the topological structure can not be flexible as the causal structure is, but one must have a free outlook on all topological possibilities before one can decide by the testimony of experience which of them is realized by our actual world. To that end one turns to topology. There the topological scheme is bound only by certain axioms; but the topologist derives numerical characters from, or establishes universal connections between, arbitrary topological schemes, and again this is done by explicit construction into which the arbitrary schemes enter as variables. Wherever axioms occur, they ultimately serve to describe the range of variables in explicitly constructed functional relations.

So much about the first alternative. We turn to the opposite view, which subordinates construction to axioms and deduction, and holds that mathematics consists of systems of axioms freely agreed upon, and their necessary conclusions. In a completely axioma-

tized mathematics construction can come in only secondarily as construction of examples, thus forming the bridge between pure theory and its applications. Sometimes there is only *one* example because the axioms, at least up to arbitrary isomorphisms, determine their object uniquely; then the demand for translating the axiomatic set-up into an explicit construction becomes especially imperative. Much more significant is the remark that an axiomatic system, although it refrains from constructing the mathematical *objects,* constructs the mathematical *propositions* by combined and iterated application of logical rules. Indeed, drawing conclusions from given premises proceeds by certain logical rules which since Aristotle's day one has tried to enumerate completely. Thus on the level of propositions, the axiomatic method is undiluted constructivism. David Hilbert has in our day pursued the axiomatic method to its bitter end where all mathematical propositions, including the axioms, are turned into formulas and the game of deduction proceeds from the axioms by rules which take no account of the meaning of the formulas. The mathematical game is played in silence, without words, like a game of chess. Only the rules have to be explained and communicated in words, and of course any arguing about the possibilities of the game, for instance about its consistency, goes on in the medium of words and appeals to evidence.

If carried so far, the issue between explicit construction and implicit definition by axioms ties up with the last foundations of mathematics. Evidence based on construction refuses to support the principles of Aristotelian logic when these are applied to existential and general propositions in infinite fields like the sequence of integers or a continuum of points. And if the logic of the infinite is taken into account, it seems impossible to axiomatize adequately even the most primitive process, the transition $n \rightarrow n'$ from an integer $n$ to its follower $n'$. As K. Gödel has shown, there will always be constructively evident arithmetical propositions which can not be deduced from the axioms however you formulate them, while at the same time the axioms, riding roughshod over the subtleties of the constructive infinite, go far beyond what is justifiable by evidence. We are not surprised that a concrete chunk of nature, taken in its isolated phenomenal existence, challenges our analysis by its inexhaustibility and incompleteness; it is for the sake of completeness, as we have seen, that physics projects what is given onto the background of the possible. However, it is surprising that a construct created by mind itself, the sequence of integers, the simplest and most diaphanous thing for the constructive mind, assumes a similar aspect of obscurity and deficiency when viewed from the axiomatic angle. But such is the fact; which casts an uncertain light upon the relationship of evidence and mathematics. In spite, or because, of our deepened critical insight we are to-day less sure than at any previous time of the ultimate foundations on which mathematics rests.

My purpose in this address has not been to show how the inventive mathematical intellect works in its manifold manifestations, in calculus, geometry, algebra, physics, etc., although that would have made a much more attractive picture. Rather, I have attempted to make visible the sources from which all these manifestations spring. I know that in an hour's time I can have succeeded only to a slight degree. While in other fields brief allusions are met by ready understanding, this is unfortunately seldom the case with mathematical ideas. But I should have completely failed if you had not realized at least this much, that mathematics, in spite of its age, is not doomed to progressive sclerosis by its growing complexity, but is still intensely alive, drawing nourishment from its deep roots in mind and nature.

# SCIENTIFIC EVENTS

## ANIMALS AND AIR RAIDS

A SPECIAL correspondent of the London *Times* writes:

A certain amount of fresh facts as to the effect of air raids on animals has now come in as a result of the appeal for information made in these columns some three weeks ago. So far as the London Zoo is concerned there is little to report. It is difficult to observe the animals' behavior at night when things are really happening. After a bad night, and during such day raids as there have been, they seem unconcerned. Almost all the society's geese are at the moment at Whipsnade, so that it has not been possible to confirm the reports that geese are peculiarly alert sentinels for air raids.

However, some very interesting reports have come in from the Maidstone Zoo. In general, the experience there has been the same as in London—the animals show no reaction to the most violent air activity or anti-aircraft fire. On the other hand, the two chimpanzees, though they do not mind the guns, stamp and shriek at the sound of the siren. And of two emus, one is indifferent to noise, but the other gets so excited at the sound of the anti-aircraft guns and rushes about so violently that fears are entertained for its safety.

A cow elephant about twenty years old is so sagacious that she hurries to her house if the anti-aircraft barrage catches her in the open, but once there does not seem to mind. Finally, one lion, normally a quiet animal, after a shell fragment hit him in his cage (doing little hurt as it had ricocheted off the bars), has become con-

ditioned to the anti-aircraft guns, starting to rip his cage to bits every time they start firing.

As regards wild birds, there is a good deal of evidence that many of the larger kinds are disturbed by the sound of bombs or anti-aircraft fire. With song-birds and other passerines, however, the chief reaction seems to be to aircraft. These are treated as if they were hawks, the birds scattering downwards and crouching to avoid detection. There are two curious exceptions to this: neither robins nor any member of the swallow tribe have been seen to pay the slightest attention to aircraft. The stories of gulls giving warning of the approach of hostile aircraft are presumably based on the same reaction: their keen senses—eyes more probably than ears—detect the aeroplanes a little before they are audible or visible to human beings.

Domestic animals vary individually. Some dogs have what may be called A.R.P. sense, and distinguish perfectly between the alert and the all-clear signals. One cat has been reported in this category; at the alert she comes indoors to take shelter, but when the raiders-passed signal is given she jumps up and scratches to be let out. She is indifferent to mere noise. Other dogs show no recognition of the difference between the sirens' signals. Again, some dogs do not mind the noise of guns and bombs, or even seem to like it, while others are miserably frightened and crawl under the furniture. Some parrots definitely dislike the noise, and scream loudly and hysterically.

## EARTHQUAKES OF 1940[1]

FOUR strong distant earthquakes were registered at Kew Observatory during September. They were on September 12, 19, 21 and 22. The second of these was the greatest, having a ground amplitude at Kew of 47 $\mu$, and being estimated at a distance of 17,400 km. The second was at a distance of 6,100 km with an estimated depth of focus of about 390 km, whilst the third, probably distant about 140°, had a depth of focus of approximately 500 km. News from other observatories is awaited before the epicenters and depths of focus can be given with precision.

On September 4, two local earthquakes were felt in Palestine each of which lasted about 10 seconds. No damage has been reported and the shocks were not registered at Kew. It is reported in the press that an earthquake was felt in Copenhagen early on September 28. No damage was reported. Earthquakes are rare in this district and the shock may have been caused by fault slipping in the Sound separating Denmark from Sweden.

The coast of Chile in the neighborhood of Iquique was shaken by a violent earthquake about 6 A.M. (local time) on October 4. Reports of damage and details of the shock are not yet to hand. Chile as a whole is very liable to earthquake shocks, and Iquique has been affected on a number of occasions in the past, notably on May 9, 1877, when there was widespread destruction due to large sea waves caused by the earthquake in addition to the extensive damage done by the earthquake itself, and on January 23, 1878.

During April, May, June, 1940, forty-seven earthquakes were registered at the Riverview College Observatory, New South Wales, as compared with fifty-six in the first quarter of the year. The observatory is equipped with two Wiechert horizontal 1,000 kgm instruments, one Wiechert vertical seismometer of 80 kgm, two Mainka 450 kgm seismometers and three Galitzin aperiodic seismometers with galvanometer registration, orientated north-south, east-west and vertical. The largest two shocks of the period appear to have been on April 1 when an amplitude of 23 mm was obtained and on May 28 when an amplitude of 22 mm was reached. The shock of April 18 was felt in the region of the Duke of York Islands, New Britain, etc. The shock of May 24 is reported to have had its epicenter in Peru, and the earthquakes of June 18 and June 22 were deep focus shocks. The instruments are occasionally affected by microseisms which are at times severe. The microseisms do not often preclude the accurate reading of the seismograms, details of which are given in the observatory report.

[1] From *Nature*.

## FINANCES OF THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY

IN the annual report of President Karl T. Compton, of the Massachusetts Institute of Technology, the finances of the institute are discussed. The institute closed the year with a modest surplus. Of the budgeted expenditure of $3,333,000, slightly more than 69.3 per cent. was for academic expenses, 26.4 per cent. for plant and administration, and 4.3 per cent. for miscellaneous expenses. The yield on all investments, based on market values as of June 30, was 4.32 per cent. as compared with 3.89 per cent. a year ago.

Financial aid to students during the year amounted to $434,966, which included undergraduate scholarships to the sum of $93,830, and graduate scholarships and fellowships reaching a total amount of $111,618. Loans to students amounted to $162,843, and $66,675 was earned through the student employment service.

Commenting upon the institute's placement service for alumni and the graduating classes, Dr. Compton reported that the class of 1940 was more than 90 per cent. placed on September 1, and that the men of this class found employment in thirty different states. A number of those not placed include graduates who are entering private consulting or architectural practice.

Among the urgent needs of the institute are a new building for the department of chemical engineering, the largest in the institute, which is now greatly overcrowded. Plans for such a building have already been

drawn and should the necessary funds be obtained, the new quarters would relieve congestion in a large part of the educational buildings on the eastern side of the institute. Attention was called to the need for new biological laboratories and the opportunities that could be realized by an increase in research funds of $200,000 a year or more.

Dr. Compton also pointed out that the large waiting list is evidence of the need of an additional dormitory unit, which could be immediately filled.

## ACQUIREMENT BY HARVARD UNIVERSITY OF A DEPOSIT OF FOSSILS IN NORTHERN FLORIDA

DR. THOMAS BARBOUR, director of the Harvard Museum of Comparative Zoology, announces that a rich deposit of fossils in Gilchrist County, northern Florida, dating back some 18,000,000 years to the Miocene era, has been purchased by Harvard University for research purposes. The deposit, on a forty-acre farm site, contains the only reasonably complete store of Miocene fossils so far reported in the United States east of the Rocky Mountains. In preliminary excavations, Dr. Barbour and members of the museum staff found remains of several primitive horses, camels, dogs and rhinoceros. The deposit is expected to give the first good picture of land-life on the eastern seaboard during the Miocene period. All other eastern Miocene deposits are primarily of marine life.

Dr. Theodore E. White, of the museum staff, will work at the site this winter under a grant from the Milton Fund of Harvard University. Several years of excavation will be required to piece together the picture of the fauna as found in the fossil bones.

Fragments from the deposit have been on exhibit for some years at the museum of the Florida Geological Survey. These were seen several years ago by Dr. Barbour, who, with the aid of Mr. and Mrs. William E. Schevill, of the museum, located the site and made preliminary excavations. Last winter Drs. Barbour and White excavated for a longer period, finding some complete skulls and long bones. The specimens found at the end of the work last winter were better preserved than those found earlier, and it is probable that further digging will disclose material still better preserved.

## EQUINE ENCEPHALOMYELITIS AND MOSQUITOES

EVIDENCE as to the guilt or innocence of mosquitoes in transmitting equine encephalomyelitis will be analyzed at the eleventh annual Conference of Mosquito Abatement Officials in California, to be held at the University of California at Berkeley, on December 16.

Speakers and their subjects, announced by S. F. Dommes, Jr., secretary, are as follows:

*Epidemiology and Distribution of Human Cases*, Dr. H. L. Wynns, chief, Bureau of Epidemiology, California State Department of Public Health.

*Distribution of Cases in Horses and the Economic Importance of Equine Encephalomyelitis in Horses*, Dr. C. U. Duckworth, administrator, Division of Animal Industry, California State Department of Agriculture.

*Relationship of Distribution of Cases and Mosquitoes*, Thomas H. G. Aitken, University of California.

*Investigations of Equine Encephalomyelitis in Kern County*, Dr. W. C. Buss, epidemiologist, Kern County Health Department.

*Present Information on Experimental Transmission of Equine Encephalomyelitis by Mosquitoes*, Dr. Malcolm H. Merrill, California State Department of Public Health.

Professor W. B. Herms, head of the Division of Entomology and Parasitology of the University of California, will introduce the symposium, and a summary of the discussion is to be presented by Dr. Bertram P. Brown, director of the California State Department of Public Health.

Representatives from twenty-five mosquito abatement districts and from health departments and universities in California ordinarily attend the conference. This year, invitations have also been sent to state universities and health departments in Washington, Oregon, Montana, Idaho, Nevada, Utah, Arizona, Colorado and New Mexico.

Methods of organizing mosquito abatement districts, experiences in mosquito control as a health department function and various operating problems will also be considered at the conference. William Reeves, a graduate entomologist at the University of California, will report on research on the Pacific Coast "tree-hole" mosquito, *Aedes varipalpus*.

## THE ROLE OF DENTISTS IN NATIONAL DEFENSE

THE American Dental Association at its recent meeting in Cleveland used as a general theme the national defense and the special role of the dental profession in it. A nation-wide dental health census, conducted by the Committee on Economics, indicated that "the nation, from a dental standpoint, is woefully unprepared to meet the exacting requirements in industry and the military services in a time of possible national emergency." Although the data from this survey have not been entirely worked over, Dr. R. M. Walls, chairman of the Committee on Economics, told the House of Delegates of the association that "after careful consideration of the figures now available, we must face the fact that an immediate effort must be made by dentistry to meet a situation which may have a serious effect on the whole defense program."

Because of the national condition thus indicated, and drawing on experience in the last war concerning

dental health in the army and in industry, the American Dental Association adopted a three-point program to mobilize America's dental resources for national defense as follows:

(1) Sending to every registered dentist in the nation a questionnaire giving complete information on the dental personnel available for military purposes and for civilian needs.

(2) Launching a program for cooperation with the Surgeon-General of the Army and Navy to reduce the percentage of rejections for dental defects among volunteers and prospective draftees under the conscription law.

(3) Setting in motion a special education program for dentists by distributing courses in military dentistry now under preparation by the War Department.

## MEMORIALS

EXERCISES in honor of the centennial of the death of Constantine Rafinesque were held at Transylvania College, on October 30. An address was given before the student convocation by Dr. Francis W. Pennell, of the Philadelphia Academy of Natural Sciences, and at the luncheon by Dr. A. E. Emerson, of the University of Chicago, who spoke on "The Modern Naturalist." In the afternoon there was a symposium entitled "Rafinesque's Interests—a Century Later," at which Dr. W. D. Funkhouser, of the University of Kentucky, spoke on "Archeology in Kentucky"; Dr. W. E. Ricker, of Indiana University, on "Research in the Biology of Fish" and Dr. W. M. Clay, of the University of Louisville, on "Herpetology." At the dinner addresses were given on "The Life and Works of Rafinesque" by Dr. Francis W. Pennell, and on "Constantine Rafinesque, the Man," by Dr. L. R. Dingus. The remains of Rafinesque were removed from Philadelphia in 1923 and were placed in a crypt on the campus of Transylvania College. The college has in its possession a collection of the manuscripts, books and letters, and two of the three known portraits of Rafinesque.

WASHINGTON AND JEFFERSON COLLEGE, Washington, Pa., dedicated on October 26 a new building for chemistry to the memory of Dr. Jesse W. Lazear, who died in Cuba in 1900 of yellow fever while serving as a member of the Yellow Fever Commission of the U. S. Army. Dr. Lazear was an alumnus of the college. John R. Kissinger, Huntington, Ind., and John J. Moran, Habana, Cuba, two of the group of soldiers who allowed themselves to be bitten by mosquitoes during the investigation, were guests at the dedication ceremonies. At a banquet in the evening Dr. Philip S. Hench, of Rochester, Minn., made an address on the work of the Yellow Fever Commission. The Jesse W. Lazear Chemistry Hall is one of three buildings dedicated. One of these was named in honor of the late Dr. Edwin Linton, for many years professor of biology and geology at Washington and Jefferson College.

THE "Cradle of Dental Education in America" will be dedicated on November 24 by the Ohio State Dental Society at Bainbridge. This dental monument is a small brick building which served as the office of Dr. John Harris from 1825 to 1850. It has been purchased and restored by the society and will be maintained as a permanent museum and memorial. Addresses will be given at the dedication by Dr. B. W. Weinberger, Dr. Arthur H. Merritt and Dr. J. Martin Fleming. Dr. Harris served as preceptor to a group of students, several of whom later became prominent in dental education and practice. Dr. Chapin A. Harris received his dental training at the Ohio State University and then went to Baltimore. There he and Dr. Horace Hayden founded, in 1840, the first chartered dental college in the world, the Baltimore College of Dental Surgery. Dr. James Taylor also secured his dental training under Dr. John Harris and in 1845 founded the second dental college. This was the Cincinnati College of Dental Surgery whose influence was, perhaps because of its central location, more far-reaching than that of the Baltimore School.

# SCIENTIFIC NOTES AND NEWS

DR. HENRY E. SIGERIST, professor of the history of medicine and director of the Institute of the History of Medicine at the Johns Hopkins School of Medicine, and Dr. Esmond R. Long, professor of pathology at the University of Pennsylvania and director of the Henry Phipps Institute, have been elected honorary members of the athenaeum of the chair of the history of medicine in Buenos Aires.

ON the occasion of the installation of President Kenneth Irving Brown at Denison University on October 18, the degree of doctor of science was conferred on Daniel Sheets Dye, who has been head of the department of science at Union University, Chengtu, West China, since 1910.

CITATIONS of merit have been awarded by the Park Association of New York City for "outstanding service" to the parks of the city. The nine awards made included one to Dr. W. Reid Blair, who retired as director of the New York Zoological Park last May. Dr. Blair joined the staff of the park in 1902, and was appointed director in 1926. The citation said that for thirty-eight years he had carried out his work at the New York Zoological Park with "untiring zeal and devotion."

*Nature* states that the Academy of Sciences of the USSR has awarded the Pavlov Prize for 1940 to Professor Maria K. Petrova, of the Pavlov Institute of Physiology and the Institute of Evolutionary Physiology and Pathology of the Higher Nervous Activity, who is known for her study of experimental neuroses, their mechanism and therapy. The annual Pavlov Prize of 20,000 roubles, for the best work in the field of physiology, was instituted by the Soviet Government in 1936.

DR. FREDERICK B. HUTT, professor and head of the department of poultry husbandry and animal genetics at Cornell University, has been appointed head of the department of zoology in the College of Agriculture and professor of zoology and chairman of that department in the College of Arts and Sciences. Dr. Herbert Bruckner has been appointed acting head of the department of poultry husbandry.

DR. LYMAN E. JACKSON, junior dean of the College of Agriculture of the Ohio State University, has been elected president of the South Dakota State College of Agriculture and Mechanic Arts at Brookings. He will also be head of the South Dakota Agricultural Experiment Station and of the Agricultural Extension Service.

CHANGES in the department of physics of Harvard University are as follows: Professor G. W. Pierce has retired and Professor E. L. Chaffee has taken his place as director of the Cruft Laboratory. Professor N. H. Black has also retired. Professor F. A. Saunders has resigned the chairmanship of the department and Professor E. C. Kemble has been appointed to succeed him.

PROFESSOR GERTRUDE M. COX, of the Statistical Service of the Iowa State College, has become director and head of a newly organized laboratory of experimental statistics at North Carolina State College.

DR. R. C. ERNST, professor and head of the department of chemical engineering, has been appointed director of the Division of Industrial Research at the Speed Scientific School of the University of Louisville, Kentucky.

JOHN G. DEAN recently resigned his position with the Permutit Company as director of the Laboratory Research Division to become a member of the science faculty of Sarah Lawrence College, Bronxville, N. Y.

THE following appointments have been made at Parsons College, Fairfield, Iowa: Dr. J. R. Jenness, of the College of the Ozarks, head of the department of physics and mathematics; Dr. S. Porter Miller, of Buena Vista College, head of the department of chemistry; Dr. J. W. Hancock, of Michigan City, Ind., High School, assistant professor of psychology; Miss Louise Reed, Westphalia, Kans., High School, head of the department of home economics; Malcolm McDonald, of the State University of Iowa, assistant professor of biology.

DR. W. A. CLEMENS, director of the Pacific Biological Station at Departure Bay, Canada, has been appointed head of the department of zoology of the University of British Columbia.

DR. ANTONIO G. SISON, dean of the College of Medicine, has been appointed director, and Dr. Agerico B. M. Sison, assistant professor of medicine, secretary, of the newly established Post-Graduate School of the College of Medicine of the University of the Philippines.

DR. THOMAS F. ANDERSON, instructor in physical chemistry at the University of Wisconsin, has been awarded the RCA Electron Microscope Fellowship. In collaboration with the Fellowship Committee, by whom he was appointed, Dr. Anderson will devote a year to research at the RCA Research Laboratory at Camden, N. J., with the electron microscope which was recently developed in the research laboratories of the corporation, and has now been made available for research workers. Dr. Stuart Mudd, of the School of Medicine of the University of Pennsylvania, is chairman of the committee of award. Other members are Dr. M. Demerec, Station of Experimental Evolution, Carnegie Institution of Washington; Dr. J. H. Kempton, U. S. Bureau of Plant Industry; Dr. C. W. Metz, department of zoology, University of Pennsylvania; Dr. W. M. Stanley, Rockefeller Institute for Medical Research, Princeton, N. J.; Dr. Caryl P. Haskins, Haskins Laboratories, and Dr. V. K. Zworykin, RCA Research Laboratories. The terms of the fellowship provide for investigation of biological problems with the RCA electron microscope, and for experimentation to develop techniques for obtaining the fullest benefits from the electron microscope.

THE Institute of Medicine of Chicago announces that the Elizabeth McCormick Child Research Grant of $1,500 for 1940–41 has been divided among Dr. Clayton J. Lundy, Dr. Mila I. Pierce and Dr. Heyworth N. Sanford for the continuation of the investigations begun under their 1939–40 grants, Dr. Lundy's on heart sound records in rheumatic heart disease, Dr. Pierce's on leukosis, and Dr. Sanford's on the role of qualitative platelet factors in the coagulation of the blood.

F. G. FRIEDLANDER, who was born in Germany, but was educated in England, has been elected to a fellowship at Trinity College, Cambridge, for his contributions to mathematics. Mr. Friedlander is at present interned in Canada, on account of his German origin.

DR. JOHN B. YOUMANS, associate professor of med-

icine and director of postgraduate instruction in the School of Medicine of Vanderbilt University, who has leave of absence to serve as a member of the Health Commission of the Rockefeller Foundation, has sailed for Europe. Dr. Youmans will serve as dietitian in charge of the nutritional phases of the health program of the commission. The work of this commission, consisting of six or eight specialists in medical and health fields, will be to aid the French in reestablishing and reorganizing the health service of that country.

DR. DANIEL MELNICK, of the University of Michigan, has been appointed chief chemist of the Food Research Laboratories, Inc., of which Dr. Philip B. Hawk is director.

DR. MELVILLE T. COOK, plant pathologist at the Agricultural Experiment Station at Rio Piedras, Puerto Rico, who retired on July 1, will make his headquarters for the present with his son, Dr. Harold T. Cook, at the Virginia Truck Experiment Station at Norfolk, Va.

DR. HENRY E. SIGERIST, director of the Institute of the History of Medicine at the Johns Hopkins University, is delivering at Cornell University a series of six Messenger Lectures on "Civilization and Diseases."

DR. EDWARD L. THORNDIKE, professor emeritus of psychology at Teachers College, Columbia University, gave on November 13 a lecture entitled "The Development, Retention and Attraction of Superior Men" at a meeting of the American Academy of Arts and Sciences.

PROFESSOR ROBERT S. WOODWORTH, of Columbia University, will give an address entitled "Recent Results on Heredity and Environment" at a meeting to be held at the American Museum of Natural History on November 18 of the Section of Psychology of the New York Academy of Sciences.

DR. QUINCY WRIGHT, professor of international law at the University of Chicago, gave an address on October 31 at a joint meeting of the Chicago branch of the American Association of Scientific Workers and the Midwest Association of Sigma Xi. He spoke on "The Influence of Invention on Warfare."

DR. KARL K. DARROW, of the Bell Laboratories, Inc., of New York, addressed the student body of Rutgers University on November 13 on the occasion of the second of the series of seven convocations celebrating the one hundred and seventy-fifth anniversary of its founding. He spoke on "New Radio-Active Substances Produced by Transmutation." In the afternoon a symposium was conducted by Dr. Darrow, at which members of the faculties of the science departments, advanced students, physicists from industrial organizations in the vicinity and from neighboring colleges and universities were present.

THE second annual meeting of the Sigma Xi Club of Hawaii was held on October 18 at the University of Hawaii. Election of seven new members brought the membership up to seventy. New officers elected for the ensuing year are: *President,* Dr. C. H. Edmondson, professor of zoology, University of Hawaii; *Vice-president,* Dr. J. H. Beaumont, director, Hawaii Agricultural Experiment Station; *Secretary-treasurer,* Dr. S. S. Ballard, assistant professor of physics, University of Hawaii; *Councilors,* C. E. Pemberton, executive entomologist, Experiment Station of the Hawaiian Sugar Planters' Association; Dr. J. L. Collins, geneticist and acting director, Experiment Station, Pineapple Producers Cooperative Association, and Dr. C. J. Hamre, *ex-officio,* professor of zoology, University of Hawaii. The address of the evening was given by the retiring vice-president, Dr. Martha Potgieter, associate nutritionist, of the Hawaii Agricultural Experiment Station. She spoke on "The Family Diet and Its Relation to Child Health," a report of the findings to date of the Nutrition Department of the Hawaii Agricultural Experiment Station regarding local food habits, adequacy of family diets and possible effects of dietary deficiencies on the physical and dental status of children in Hawaii.

THE fourteenth annual meeting of the Colorado-Wyoming Academy of Science was held on October 18 and 19 at the University of Wyoming. One hundred and twenty-five papers were presented. President Roy M. Green, of the Colorado State College of Agriculture and Mechanic Arts, gave the main address, which was entitled "A Scientific Approach to Agricultural Problems." The newly elected officers are: *President,* Dr. C. T. Hurst, Western State College, Gunnison; *Vice-president,* Dr. Wm. Warren Howe, Colorado School of Mines, Golden; *Executive Secretary,* Dr. Essie White Cohn, University of Denver, and *Treasurer,* Dr. Charles F. Poe, University of Colorado.

IN order to ensure opportunities for the publication of the scientific results of cancer research, a group of representatives of interested organizations will cooperate in making possible a new journal, to be called *Cancer Research,* to be devoted to articles and abstracts of articles having to do with cancer research. This journal is sponsored by the American Association for Cancer Research, the Anna Fuller Fund, The International Cancer Research Foundation and The Jane Coffin Childs Memorial Fund for Medical Research. The conduct of the journal will be in the hands of an Advisory Board consisting of the chairman of the editorial committee and representatives of the con-

tributing Funds, an editorial committee and a business manager. Those serving are: *Advisory Board:* S. Bayne-Jones, representing The Jane Coffin Childs Memorial Fund for Medical Research; C. C. Little, as chairman of the Journal Committee of the American Association for Cancer Research; James B. Murphy, as chairman of the Editorial Committee of *Cancer Research;* Mildred W. S. Schram, representing The International Cancer Research Foundation, and G. M. Smith, representing the Anna Fuller Fund. *Members of the Editorial Committee* are: James B. Murphy, *chairman;* S. Bayne-Jones, for immunology and the viruses, and secretary of the committee; John Bittner, for genetics; Alexander Brunschwig, for physiology; L. F. Fieser, for organic chemistry; Jacob Furth, for the leukemias; W. U. Gardner, for hormones; Balduin Lucké, for general biology, including tissue culture and cytology; M. J. Shear, for biochemistry, and Shields Warren, for pathology. The business manager is A. Vaughn Winchell, American Oncologic Hospital, Philadelphia. It is hoped to start publication with the issue of January, 1941. Manuscripts should be addressed to the Secretary of the Editorial Committee, 333 Cedar Street, New Haven, Conn.

A "Bibliography on Arthogonal Polynomials" has been published as a Bulletin of the National Research Council. A Committee of the council, consisting of Professors Hille (Yale), Shohat (Pennsylvania), and Walsh (Harvard) has spent several years in the compilation of the bibliography, with the cooperation of several other mathematicians here and abroad. The Faculty Research Committee of the University of Pennsylvania and its Sigma Xi Chapter has given financial aid.

THE British Royal College of Physicians has announced that the Harveian Oration, the Bradshaw, the Fitzpatrick and the Lumleian Lectures for 1940 have been postponed.

IN spite of the war, the Engineering Societies Library reports that it is experiencing no difficulty in its receipt of technical periodicals from Great Britain. However, only a few engineering magazines reach the library now from continental Europe. The three hundred and fifty or more periodicals from England and other parts of the British Empire are coming through with unusual regularity except in one or two instances since the beginning of the war when the ship carrying a batch of them was sunk by a torpedo or a mine. However, correspondence with the publishers soon brought replacements for all lost copies. The Allied blockade of Germany failed to stop the flow of German magazines to the library through Italy. But, with the entrance of the latter country into the war, the library failed to receive German and Italian publications for several months. Now, some of the German periodicals are being received again through Siberia and Japan, as indicated by the postmarks on the wrappers. *Genie Civil* and other French periodicals ceased arriving a few weeks after the surrender of France. To avoid the loss of valuable publications being sent to and received from the British Isles and continental Europe through exchange agreements between engineer institutions there and the Engineering Societies Library and its cooperating organizations, arrangements have been completed to store them in the country of origin until the end of hostilities. Similar arrangements during the world war proved so satisfactory that only one or two sets of foreign periodicals failed to be completed with the resumption of commerce between belligerents.

# DISCUSSION

## CORAL-REEFS AND THE FORMATION OF PETROLEUM

IN his recent article on the "Progress in Petroleum" Egloff[1] has presented a brief discussion of a theory of continual petroleum formation from marine sediments, as for example diatoms, foraminifera and radiolaria. In reference to this theory the preliminary results of investigations which are in progress in this laboratory may be of some interest, because they indicate that coral-reefs should also be taken into consideration as one of the possible sources of petroleum.

Reef-building corals contain a by no means inconsiderable quantity of organic material. One hundred years ago, Silliman[2] in his classical paper on the composition of stony corals has stated that the organic matter of various corals amounted to from 4 to 8 per cent. of the total, and that it was intimately united with the inorganic material throughout the structure of the coral. Silliman's observations have been verified in recent years by Clarke and Wheeler[3] (1922), who found that the organic matter of twenty-eight species of corals amounted to from 2 to 7 per cent. It is also of considerable interest that Silliman called attention to the fact that part of the organic matter consists of some wax-like material which can be separated from its inorganic surroundings by boiling with water. After the boiling of the corals it was found floating on the surface of the water in "transparent, jelly-like masses of yellowish color. It was insoluble

[1] G. Egloff, SCIENCE, 91: 533, 1940.
[2] B. Silliman, *Am. Jour. Sci.*, (2) 1: 189, 1846.
[3] F. W. Clarke and W. C. Wheeler, *U. S. Geol. Surv. Paper* No. 124, Government Printing Office, Washington, 1922.

in alcohol, but readily so in cold ether, and the evaporation of its ethereal solution yielded a yellow solid, resembling wax." Since Silliman's time practically no work has been done on the organic constituents in corals, which is rather surprising because the reef-building corals occur in almost unlimited abundance in the coastal regions of tropical waters.

In the course of a systematic study of the steroids of lower marine animals, the lipoid fractions of a number of stony- or reef-corals (Madreporaria) and sea-fans (Gorgonaceae) were prepared at this laboratory. It was found that these fractions represent a not inconsiderable proportion of the starting material. In the case of the staghorn coral, *Madrepora cervicornis,* concentration of its acetone extract led to the precipitation of a low-melting, crystalline, wax-like material in a yield of about 0.25 per cent. of the total mass of corals. After frequent recrystallizations the wax melted at 50–50.5°; it was identified as pure cetyl palmitate. The remaining extracts of the coral were saponified, and the non-saponifiable fraction, which amounted to 0.25 per cent. of the total, was separated into three fractions containing the following groups of compounds: (A) sterols precipitable with digitonine, (B) non-steroid alcohols, and (C) non-alcoholic compounds like hydrocarbons and ketones. Fraction A consisted of a mixture of sterols containing at least one unknown sterol giving an acetate of m.p. 176°. Fraction B consisted almost exclusively of cetyl alcohol and fraction C of low-melting hydrocarbons and small amounts of ketones. Similar results were obtained with the coral *Meandra areolata,* which contained about 0.3 per cent. non-saponifiable material consisting of cholesterol, an unknown sterol, cetyl alcohol, hydrocarbons and possibly some ketones. The results so far available indicate that stony corals contain from 0.3 to 0.5 per cent. of non-saponifiable material or about 10 per cent. of the total amount of organic material present.

The sea-fans (Gorgonaceae) which also contribute to reef formation are much more abundant in non-saponifiable material than the stony corals. In certain species the calcareous outside layers contain as much as 3 per cent. For example: 1,000 g. of dried and crushed external layers of a brown Gorgonia from Florida gave 33 g. of non-saponifiable material or 3.3 per cent. It consisted of about 20 per cent. of an unknown sterol, 50 per cent. of alcohols (cetyl alcohol) and 30 per cent. of semi-solid hydrocarbons. 1,100 g. of layers of a yellow Gorgonia gave 2 per cent. of non-saponifiable material consisting of about 30 per cent of an unknown sterol, 30 to 40 per cent. of other alcohols and the remainder of a mixture of hydrocarbons and possibly ketones which was liquid at room temperature. The compounds described can be isolated equally well from dried, but unbleached old museum specimens as from freshly collected material.

The presence of such sizable quantities of lipoid material in reef-building animals seems rather significant. It is not confined, as has already been pointed out by Silliman, to the relatively thin living layer, but extends deep into the entire structure of the coral. In view of these findings the idea at once suggests itself that coral reefs may act as gigantic accumulators of "wax-like" substances, especially of the chemically inert hydrocarbons. The bulk of the organic matter of dead marine animals and plants is probably brought back into circulation one way or the other. In the case of the reef-building animals, however, a significant portion of the organic matter becomes trapped in the ever-growing inorganic skeleton and hence is removed from further circulation. If this is indeed the case we must conceive the coral reefs as vast storehouses of compounds which may be considered as potential precursors of petroleum. At some time changes in the physical conditions may loosen this material from its inorganic surroundings and bring it to the surface, similar to the wax-like material which Silliman found floating on the surface of water in which corals had been boiled. The authors of the present article are not petroleum chemists and they do not claim the complicated problem of the formation of petroleum can be solved merely on the basis of the coral reefs. They present their preliminary findings only in order to call attention to the coral-reefs as one of the possible sources of petroleum and to stimulate discussion along this line.

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## THE OCCURRENCE AND ISOLATION OF AZOTOBACTER IN CHINESE SOILS[1]

ON account of their relation to soil fertility, the non-symbiotic nitrogen fixation bacteria, Azotobacter, have received considerable attention since their discovery by Beijerinck in 1901. They are widely distributed in the soils throughout the world, as their occurrence has been reported in the soils of Java, India, Poland, the United States, England, Japan, Russia, etc. The only country whose soils are completely devoid of this microorganism is Finland.[2] As yet, however, there is no information about their occurrence in the vast area of Chinese soils.

The purpose of the present study is to make a general survey of the occurrence of Azotobacter in the soils of Szechuen Province, which, under the present circumstances, is probably the most important agricultural region in China. The work also involves the

[1] The detailed report of this work will appear in *Soil Bulletin* (bimonthly publication, National Geological Survey, Ministry of Economics, China).

[2] W. Brennar, *Geol. Komm. Finland Agrogeol. Meddel.,* 20: 1–15, 1924.

isolation of pure cultures from the soils for experimental works which the writer is planning to carry out in the near future.

The soil samples, including as many as fifteen or more types, were collected under more or less sterile conditions from various parts of the province, particularly the northwestern section. They are composite samples taken from the soils at a depth of about 20 to 30 cm below the surface.

The presence of Azotobacter in the soils was determined by using mannitol, dextrin or other simple carbohydrates in liquid media, and the results so obtained were checked by using either the nitrogen-free nutrient agar medium of Martin, Walker and Brown[3] or soil plaque methods of Winogradsky.[4] As a rule, two or three independent determinations were made for each sample.

Of all the 127 soil samples collected and determined, 102 or 78.2 per cent. contained Azotobacter. This finding is not surprising in view of the fact that in other countries over 50 per cent. of the soils containing Azotobacter is not uncommon, as reported by various workers, and furthermore, the soils of Szechuen Province are well known to be very fertile.

Isolation of the pure cultures was carried out during the progress of the survey. The media used were nitrogen-free agar media of various kinds. Repeated purifications were made by using congo red nitrogen-free agar medium of Bryan.[5] This medium proves to be very useful in purification especially in separating Azotobacter from their most common contaminants, Radiobacter.

The strains isolated from this survey are mostly *Azotobacter chroococcum* although a few of them are not yet definitely identified.

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## PRODUCTION OF SYMPTOMS BY SUBCUTANEOUS INJECTION OF HISTAMINE WITHOUT INCREASE OF THE BLOOD HISTAMINE[1]

HISTAMINE has been used to produce experimental shock by many investigators, and at one time it was thought to be one of the toxic factors responsible for the production of shock following trauma. Since it was impossible to detect histamine in the circulating blood under these conditions, this substance was rejected as a possible cause by many workers. It was stated that when symptoms of shock were produced by the injection of histamine, large amounts of this substance were present in the circulating blood and therefore easily detectable.[2]

In order to note the changes in the blood histamine following the production of symptoms by the subcutaneous injection of this substance, the following procedure has been carried out in ten patients. A control blood is taken, blood-pressure and pulse being noted. One mgm of histamine diphosphate is then injected subcutaneously and the blood histamine determined, at 5, 15, 30 minutes and one hour, blood-pressure and pulse being recorded at the same time. In each instance symptoms of histamine intoxication were noted, such as an increase in pulse, decrease in blood-pressure, flushing of the face and the onset of headache. In no case, however, was an increase of blood histamine observed, even at the height of the symptoms. It was also noted that the particular allergic symptoms were reproduced if the patient on whom the test was being carried out was an allergic individual. The relationship of blood histamine to allergy is being reported elsewhere.[3]

In the light of these findings, therefore, it appears that histamine intoxication may occur without an increase in the peripheral blood histamine. Failure to demonstrate an increase in the peripheral blood histamine does not exclude the possibility that this substance may be responsible for the symptoms of shock.

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## AGASSIZ AND LIEBIG

THE year 1940 should not be allowed to pass without noting that it marks the centenary of the publication of two papers whose contents have profoundly influenced the history of agronomy and of its offspring, soil science. These papers were "Etudes sur les glaciers," in two volumes, by the Swiss naturalist Louis Agassiz, and "Die Chemie in ihrer Anwendung auf Agriculture und Physiologie" by the German chemist Justus von Liebig.

Born within a few hundred miles of each other, the lives of these scientists were contemporaneous and almost conterminous. Agassiz, by his glacial hypothesis, solved the riddle of the origin of the surficial deposits of a large portion of the northern hemisphere. Liebig, with his mineral theory of plant nutrition, gave the world the scientific basis for the use of mineral fertilizers. Both men greatly stimulated research in their respective fields. Agassiz traveled in America, and liked the United States so well that he accepted the offer of a professorship in Harvard University and settled in this country.

A. B. BEAUMONT

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[3] Martin, Walker and Brown, *Research Bull.* 217, Iowa Agr. Exp. Sta., 1937.
[4] S. Winogradsky, *Ann. Inst. Pat.*, 40: 455–520, 1926.
[5] C. S. Bryan, *Soil Science*, 45: 1938.
[1] Aided by a grant from the Banting Research Foundation.

[2] C. A. Dragstedt and F. B. Mead, *Jour. Am. Med. Asn.*, 108: 95, 1937.
[3] *Journal Allergy* (in press).

# THE NATIONAL ACADEMY OF SCIENCES

## ABSTRACTS OF PAPERS

(*Continued from page 419*)

*The establishment of precise spectrophotometric constants for hemochromogens and Cytochrome C, upon an iron basis, and the analysis of the Cytochrome C spectrum:* DAVID L. DRABKIN[1] (introduced by W. M. Clark). A new method[2] has been modified appropriately and adapted successfully to the accurate determination of iron in such organic complexes as hemin and Cytochrome C. The iron, freed from the complex and reduced under controlled pH conditions, is converted into ferrous orthophenanthroline, which has an absorption maximum at wave-length 500 mμ. The light transmission (from which the extinction is calculated) was determined by precise, visual spectrophotometry, or by means of a photoelectric filter photometer of new design (to be described elsewhere). 10 mg samples of Cytochrome C, the purest preparations of which contain 0.43 per cent. iron, were sufficient for accurate analysis. The precision of the method was equal to that of spectrophotometry under optimal conditions. Using the iron content as the basis for the concentration of total pigment, spectrophotometric constants, $\varepsilon$[3] (C = 1 mM per liter (iron equivalent basis), d = 1 cm, spectral interval = 1.5 to 2 mμ), were established for dipyridino ferroporphyrin (a synthetic hemochromogen) and Cytochrome C.

*The kinetics of the enzyme-substrate compound of peroxidase and their relation to the Michaelis theory:* BRITTON CHANCE, J. G. BRAINERD, F. A. CAJORI and G. A. MILLIKAN (introduced by A. N. Richards). A study of the kinetics of the formation and breakdown of the enzyme-substrate compound of peroxidase has been carried out by means of a photoelectric method for measuring rapid changes in the violet absorption spectrum of the enzyme. Under the same conditions, photoelectric measurement of changes in the red absorption spectrum of malachite green were recorded as leuco-malachite green was oxidized by peroxidase and hydrogen peroxide. The complete cycle of enzyme operation was recorded: the rapid formation of the enzyme-substrate compound, the enzyme operation at constant concentration of enzyme-substrate compound and the decrease in concentration of this compound when the substrate was used up. Correspondingly, the rate of formation of malachite green started slowly, accelerated to a large constant value, and then fell to zero. Thus the operation of the enzyme-substrate compound has been directly related to the overall enzyme action. The Michaelis affinity for peroxidase, determined by direct measurement of the concentration of enzyme-substrate compound as a function of substrate concentration, was found to be in agreement with the values obtained elsewhere by measurement of the rate of malachite green formation. Solutions of the differential equations representing the Michaelis theory were obtained by the University of Pennsylvania differential analyzer and fitted the observed data in curve shape, time scale and concentration values over a part of the experimental range.

*The synthesis of chroman derivatives:* RALPH CONNOR and PETER L. DE BENNEVILLE (introduced by M. H. Jacobs). The synthesis of chromans received relatively little attention until it was discovered in 1938 that the tocopherols (Vitamin E) were chroman derivatives. In the last two years the chemistry of this series has been studied in a number of laboratories with the result that good methods are now available for the synthesis of 2,2-dialkylchromans. These methods, however, are not applicable to the synthesis of chromans with substituents in the *3* and *4* positions. The present report describes a new synthesis of chromans which should be applicable to the synthesis of any chromans except those with substituents in the *2* position. The hydrogenation of coumarin over copper chromite at 250° and under a hydrogen pressure of 2,000–3,000 pounds per square inch gave o-(γ-hydroxy-propyl)-phenol (85–90 per cent.). This phenolic alcohol, upon treatment with phosphorus tribromide, gave chroman (85–90 per cent.). By the application of this method to substituted coumarins, 4,7-dimethylchroman, 6-methylchroman, 7-methylchroman, 7,8-benzochroman and 7,8-tetrahydrobenzochroman were obtained. From 4-methyl-6-hydroxycoumarin the product was 4-methyl-6-hydroxy-hexahydrochroman. When nickel was used as a catalyst at 250°, hydrogenated chromans were the chief products obtained from coumarins. This is the first synthesis of compounds of this type. By this method the completely hydrogenated derivatives corresponding to all the chromans named above were isolated. These results indicate that coumarins, which are fairly readily prepared by known methods, may be readily converted to either chromans or hexahydrochromans by selection of the appropriate catalyst.

*Sulfonyl ureas:* EDWARD H. COX (introduced by C. E. McClung). Only two methods for the preparation of sulfonyl ureas are recorded in the literature. One, the ammonolysis of sulfonyl isocyanates is dangerous to carry out and gives low yields of desired product, the second, the reaction of potassium cyanate on sulfonamides is not duplicatable. We, therefore, set out to find our own method. Attempts to treat urea with sulfonyl chlorides under varying conditions, acid and alkaline ($Ba(OH)_2$) hydrolysis of sulfonyl quanidines, and acid hydrolysis of sulfonyl alkylthioureas, failed. Ammonolysis of sulfonyl urethanes also failed. We have found that the sulfonyl alkyl isoureas can be hydrolyzed to the ureas in good yields. The base, ethyl isourea is prepared as the hydrochloride salt when cyanamide dihydrochloride and cyanamide is treated with ethyl alcohol under pressure. The sulfonyl isoureas are prepared by treating the sulfonyl chloride and the isourea salt with the proper amount of alkaline solution. The sulfonyl isoureas are then hydrolyzed to the corresponding ureas by hydrochloric acid.

[1] Fellow of the John Simon Guggenheim Memorial Foundation at the Department of Physiological Chemistry, Johns Hopkins School of Medicine. Part of this work was done during tenure of the fellowship.

[2] O. Schales, Personal communication. W. Lintzel, *Z. ges. exp. Med.*, 86: 269, 1933. G. Barkan and B. S. Walker, *Jour. Biol. Chem.*, 131: 447, 1939; 135: 37, 1940.

[3] $\varepsilon$, unmodified, is the symbol for *extinction* and is equal to $-\log \tau$ (*transmission*, expressed as a fraction).

This work is preliminary to the preparation of sulfonyl ureas derivatives in the sulfanilamide series.

*Mono- and polyhydroxyprogesterones:* MAXIMILIAN EHRENSTEIN and THELMA O. STEVENS (introduced by A. N. Richards). The hormones of the adrenal cortex represent hydroxyprogesterones in which the side chain of the steroid molecule carries a primary alcohol group. In addition, one or two hydroxyl groups may be attached to the nucleus. It has been possible to obtain by synthetic chemical procedures hydroxyprogesterones which are different from the naturally occurring compounds and to subject them to a physiological examination. These compounds will be briefly discussed with reference to the subject of steroid structure and biological activity.

*The gonadotropic hormone of urine of pregnancy:* SAMUEL GURIN, CARL BACHMAN and D. WRIGHT WILSON (introduced by A. N. Richards). The gonadotropic hormone of pregnancy urine has been prepared in a high state of purity. It is a glycoprotein and has been studied by physical and chemical methods. The crude hormone was obtained from fresh urine collected from women about two months pregnant by Katzman and Doisy's adsorption method on benzoic acid. This material assaying 30–50 minimal effective doses (Friedman Units) per mg was extracted with 50 per cent. ethanol at pH 6.0 and the derived product extracted with the same solvent at pH 4.8. Preparations assaying from 1,000 to 3,000 Friedman units were obtained. Further purification was accomplished by shaking a solution of the hormone with chloroform and dialyzing the resulting solution. The material obtained by precipitation with acetone had an activity of 4,000 Friedman units. All manipulations were carried out at about 0° C. Our best material was apparently well purified because it showed homogeneity in the ultra-centrifuge and the Tiselius apparatus. The protein contains 15 per cent. carbohydrate. Two thirds of the carbohydrate is galactose and one third a hexosamine. The material is unstable in dilute solution at 0° C. An approximation suggests that the minimum molecular weight is about 80,000. Comparisons of our assay method with the International Standard indicate that our preparation which assays 4,000 Friedman units per mg contains about 8,000 international units per milligram.

*Preparation of crystalline pepsin having the properties of a pure protein:* ROGER M. HERRIOTT, VICTOR DESREUX and JOHN H. NORTHROP. The three most commonly accepted tests for the purity of a protein are homogeneity in the ultra-centrifuge and in the electrophoresis cell and constant solubility. The solubility method is based on the phase rule which states that the solubility of a pure substance must be constant and independent of the amount of solid present in the system. This method is quite analogous to the classical melting point test for purity used in organic chemistry but which is not applicable to proteins. Very few proteins have been shown to be pure by all three tests. Crystalline pepsin prepared by the method originally described shows only one protein component when analyzed in the ultra-centrifuge or in the electrophoresis cell. The solubility of such preparations, however, usually varies with the amount of solid protein present, indicating the presence of more than one component. These preparations may be separated by fractional precipitation into at least two proteins of slightly different solubility and enzymatic activity. A method has been worked out for the isolation and crystallization of the more soluble of these proteins. Such preparations of crystalline pepsin have constant enzymatic activity and their solubility in several solvents is independent of the amount of solid phase present.

*A simplified procedure for isolating the polysaccharides and nucleic acid of tuberculin using electrophoresis:* FLORENCE B. SEIBERT and DENNIS W. WATSON (introduced by D. H. Tennent). A simple scheme was devised for making a rough separation of the protein, nucleic acid and polysaccharide fractions of tuberculin. The protein was precipitated from the heated culture filtrate of tubercle bacilli, grown upon synthetic medium, by half saturation with ammonium sulfate at pH– 7.0 and 5° C. On standing in the cold the filtrate deposited a sediment, designated S2. The filtrate was carefully adjusted to pH– 4.0 with hydrochloric acid, yielding a flocculent precipitate, designated S3. Alcohol (95 per cent.) was then added to the filtrate until a brown sticky mass appeared at the interface between the two liquids. This mass was further separated into two fractions; one designated S4, which was readily soluble in water, and another designated S5, which was much less soluble. To the filtrate from these, more alcohol was added to remove ammonium sulfate and the remaining solution was concentrated in vacuo to a syrup, dialyzed in an extra heavy membrane, and dried in the cryochem, yielding a product designated S6. Electrophoretic studies in the Tiselius apparatus showed that all six fractions consisted of varying proportions of nucleic acid, protein and polysaccharide, a variance which probably accounted for their different physical properties. Chemical analyses confirmed the conclusions. Two types of polysaccharides were isolated in a Tiselius macroelectrophoresis cell, as well as by chemical separations. One type, which predominated in the S6 fraction, was immobile, homogeneous, colorless and contained only about 0.2 per cent. nitrogen. The other polysaccharide had a low mobility and was present in much larger quantities in the S4 fraction; its nitrogenous content, consisting of protein and nucleic acid, could never be reduced to less than 1.6 per cent. nitrogen, even by prolonged electrophoresis. Moreover, the component always remained diffuse, indicating that it is probably not a true compound. Pure nucleic acid was also isolated in the macroelectrophoresis cell.

*Concerning the internal organization of the streptococcal cell:* STUART MUDD (introduced by O. T. Avery). New insight is being gained into the structure of the bacterial cell through the use of the new electron microscopes available at the RCA Laboratories. The chain structure of the hemolytic streptococcus, for instance, is seen to be due to the continuity from cell to cell of a solid surface membrane which is differentiated from an interior protoplasm. Cytolysis, as, for instance, under the action of sonic vibration, may cause this inner protoplasm to escape, leaving an empty membrane analogous to the stroma of a hemolyzed red cell (Mudd and Lackman). A single strain of Streptococcus pyogenes may occur in forms varying from the virulent mucoid va-

riant with its extracellular envelope, to the naked pleomorphic cell of the rough variant, which is only just recognizable as a streptococcus. Chemically the streptococcal cell has been shown by Sevag, Smolens and Lackman to be about 80 per cent. protein and nucleoprotein. From 18 to 24 per cent. of the dry weight of muccid and smooth variants is nucleic acid, and from 14 to 17 per cent. of the rough variants; of the nucleic acid 10 to 30 per cent. gives the color reactions characteristic of the desoxyribose type and the remainder the reactions characteristic of the d-ribose type. In higher animals and plants the desoxyribose type of nucleic acid is characteristically found in the nucleus and the d-ribose type in the cytoplasm—yet no indication of the existence of a nucleus within the streptococcal cell has been found nor has any phenomenon resembling karyokinesis been observed in this or other pathogenic bacterium. The nutritional requirements of the streptococcus are extremely exacting. Thus Pappenheimer and Hottle in this laboratory have found that a certain strain of streptococcus requires, besides a source of carbon and necessary minerals, several particular amino acids, and the six characterized members of the vitamin B complex—thiamin, riboflavine, pyridoxine, pantothenic acid, nicotinic acid and biotin. The metabolic potentialities of the streptococcal cell are equally complex. For instance, beside the protein, nucleic acid, carbohydrate and lipoid of its own protoplasm, the streptococcal cell has been shown to elaborate the erythrogenic toxin, a protein hemolysin, a fibrinolysin, a leucocidin and a newly detected lethal substance (Harris). The nature of the organization within a cell of only about 1 μ diameter, which makes possible such complex syntheses and transformations of matter, is not even definitely suggested by present-day knowledge.

*The relation of hereditary constitution, allergic irritability, antibody production and the development of local immunity in resistance to tuberculosis:* MAX B. LURIE (introduced by E. L. Opie). By brother and sister inbreeding of rabbit groups, under strictly similar environmental conditions, six families have been obtained in which the genetic constitution alone determines a characteristic inherited resistance to tuberculosis of each family, generation after inbred generation. Two of these families are highly susceptible to the disase. One is of exceptionally high resistance to the infection and three are intermediate in their susceptibility to tuberculosis. The fundamental variant in the disease developed by these three family groups is the degree to which the infection is limited to the portal of entry of the bacillus. In tuberculosis naturally acquired by respiratory contagion, the most resistant family confines the disease to the lungs where the infection originates and where it slowly progresses. There is little if any dissemination to the rest of the body. In the most susceptible families there is a rapid spread by the lymph and blood from the fulminating primary pulmonary lesion. The families of intermediate resistance exhibit an intermediate degree of generalization of the disease. This suggests that resistance to tuberculosis is largely a function of those constitutional factors which determines the host-parasite relationship at the portal of entry. When members of these three family groups were treated with heat-killed tubercle bacilli intracutaneously it was found that the most resistant family rapidly developed a high degree of tuberculin sensitivity, which was maintained at a high level. Likewise antibodies (agglutinins) against the tubercle bacillus soon appeared in the blood and attained a considerable concentration therein. The most typical and constantly susceptible family developed allergic sensitivity very slowly. Similarly in this family, antibodies appeared in the blood later and attained a concentration considerably below that of the resistant family. The families of intermediate resistance developed tuberculin sensitivity even more rapidly than the resistant one. However, the momentum of this increment soon abated and sank below that of the resistant rabbits. The antibody production of these families was intermediate in rate and intensity between those of the most susceptible and most resistant families. If rabbits thus treated with killed tubercle bacilli are now infected with virulent living microorganisms in the skin the most resistant family develops a lesion which rapidly attains a maximum and soon heals. It quickly develops a local immunity. The mononuclear phagocytes rapidly acquire an effective capacity to inhibit the growth of the bacillus in their cytoplasm, for bacilli are rarely found in them. In the most susceptible families the local lesion develops apace with but retarded and feeble healing. The phagocytes do not acquire sufficient power to inhibit the growth of the bacilli. Their cytoplasm swarms with them. An intermediate degree of local immunity developed in the rabbit families of intermediate resistance.

*Studies on air-borne infection:* WILLIAM FIRTH WELLS (introduced by E. B. Wilson). An apparatus for study of the bacterial behavior of air has revealed a mechanism of air-borne infection leading to a hypothesis that the semi-enclosed atmospheres of our habitations provide a vehicle for the epidemic spread of contagion. *Air as a vehicle of contagion:* Evaporation of minute droplets expelled in expiratory processes enables infection to ride these droplet nuclei on air-currents. Quantitative experiments upon animals, inhaling nuclei-infected air, demonstrate the penetration of these nuclei to the depths of the lung with consequent production of disease. The transfer of nuclei infection from infector to infectee depends upon conditions of sanitary ventilation, and the equilibrium concentration predicted by the ratio of elimination to addition rate of test organisms in semi-enclosed spaces corresponds to the concentration of nasopharyngeal organisms determined by sanitary air analysis. Aggregation within the same enclosed atmosphere implies the proximity in time and space which dominates the idea of contagion, and is implied by the term "contacts." Air-borne infections thus become contagious infections. *Dynamics of epidemic contagion spread:* Contagious epidemics are characteristically dynamic, waxing or waning with infection velocity depending upon atmospheric density of susceptibles. If susceptible density depends upon immunity conferred by infection, then the magnitude of an epidemic

will be double the initial excess density of susceptibles over the "threshold density" determined by critical sanitary ventilation. *Experimentum crucis:* Bactericidal irradiation of air provides an instrument for making the experimentum crucis, *i.e.*, the effect of air disinfection upon the incidence of contagion introduced into susceptible aggregations, first to determine whether the epidemic spread of childhood contagions through aggregations of susceptible children can be prevented by raising the sanitary ventilation above a critical value. For three successive years classes in irradiated rooms of the primary department of the Germantown Friends School have been spared the epidemic spread of mumps or chicken-pox suffered by comparable classes in unirradiated rooms in each of these years. *Conclusion:* We intend to pursue the theory to scientific proof but believe that enough is now known to warrant the recommendation that ultraviolet radiation apparatus be installed in buildings designed to house large companies of men.

*Fat metabolism in diabetes mellitus:* WILLIAM C. STADIE, JOHN A. ZAPP, JR., and F. D. W. LUKENS (introduced by D. D. Van Slyke). The current theories of fat metabolism in diabetes mellitus are: 1. Knoop's hypothesis of successive beta oxidation. 2. Hypothesis of obligatory coupled ketone body-carbohydrate oxidation. (3) Fatty acids are converted by the liver into carbohydrate. Evidence in the literature and our own experiments convince us that these hypotheses are no longer tenable. That ketone bodies are utilized by the peripheral tissue of the diabetic animal was shown by four independent methods in the depancreatized cat. Therefore the depancreatized cat must oxidize ketone bodies without coupling with carbohydrate oxidation. The multiple alternate oxidation hypothesis postulates that fatty acids are simultaneously oxidized along the entire length of the chain at alternate carbon atoms with the formation of four molecules of ketone bodies per molecule of fatty acid and no acetic acid. Further experiments conformed to the hypothesis of multiple alternate oxidation rather than the Knoop hypothesis. By means of the multiple alternate oxidation hypothesis the ketone utilization in human cases of diabetes was calculated. The calculations show an abundant utilization of ketone bodies independent of carbohydrate oxidation. A new hypothesis for the metabolism of fats in the diabetic was formulated: Up to a certain level of fat catabolism (about 2.5 gm. of fat per Kg per day) fats are utilized completely and there is no ketonuria. When total fat catabolism exceeds this amount only a part of the fat is completely oxidized. The balance is excreted as ketone bodies. There is no obligatory chemical coupling of fat and carbohydrate oxidation. In further experiments with liver slices from depancreatized cat the important oxidative reactions were measured. The results show that there was no oxygen available for the conversion of fat to carbohydrate. It was concluded that the overproduction by the liver of carbohydrate from fat does not occur.

*Qualitative differences in the biological activity of adrenal cortical steroids:* DWIGHT J. INGLE (introduced by A. N. Richards). Extracts of the adrenal cortex have a number of measurable physiologic properties. They are capable of maintaining life in adrenalectomized animals, effect the distribution of electrolytes in the body, the amounts of carbohydrates in the body; they will maintain the ability of the adrenalectomized animal to work, and when administered in large amounts to normal animals will cause the atrophy of the adrenal cortices. A large number of pure compounds have been isolated from extracts of the adrenal cortex. Some of these compounds are biologically inactive and the active compounds show qualitative differences in their biologic properties. Thus it is found that those compounds which are the most active in prolonging the life of adrenalectomized animals are incapable of maintaining normal carbohydrate metabolism. On the other hand, compounds which have the greatest effect upon the carbohydrate metabolism of normal or of adrenalectomized animals are only weakly active for maintaining life and in effecting the distribution of electrolytes.

(*To be continued*)

# REPORTS

## A NEW PAN AMERICAN TREATY

"WASHINGTON, October 12—American Republics Sign Convention on Nature Protection." Such was the heading of a news release sent out by the Pan American Union. This was the announcement of the inception of an International Nature Protection Treaty designed to meet the international wildlife problems of the twenty-one American Republics. This is the first treaty of its kind ever to be proposed on this continent. It is planned to include twice as many countries as the only other International Convention of a similar nature. I refer to the London-African Convention of 1933, which included no provisions for migratory bird protection.

This Pan American Convention marks the third great cooperative step taken by the United States to further wildlife protection by international treaty on the American Continent.

In 1916 we ratified the Migratory Bird Treaty with Great Britain with respect to Canada. This treaty became effective in 1918. In 1936 we ratified a somewhat similar treaty with Mexico. In addition to these treaties we have entered into international agreements regarding seals, whaling, and fisheries. The Pan American Convention on Nature Protection and Wildlife Preservation in the Western Hemisphere covers a broad virgin field for international agreement.

It establishes a basic pattern for a scheme of parks and reserves throughout the Americas which our own experience has taught us is thoroughly sound. It

provides for appropriate protective laws for flora and fauna where inadequate ones exist. It favors cooperation in scientific field studies, the protection of migratory birds, the protection of vanishing species listed in a special annex, and the control of contraband fauna or flora protected by the laws of another country.

The following are the definitions of four categories of parks and reserves under the terms of the convention:

1. The expression *National Parks* shall denote:

Areas established for the protection and preservation of superlative scenery, flora and fauna of national significance which the general public may enjoy and from which it may benefit when placed under public control.

2. The expression *National Reserves* shall denote:

Regions established for conservation and utilization of natural resources under government control, on which protection of animal and plant life will be afforded in so far as this may be consistent with the primary purposes of such reserves.

3. The expression *Nature Monuments* shall denote:

Regions, objects or living species of flora or fauna of esthetic, historic or scientific interest to which strict protection is given. The purpose of nature monuments is the protection of a specific object, or a species of flora and fauna, by setting aside an area, an object or a single species, as an inviolate nature monument, except for duly authorized scientific investigations or government inspection.

4. The expression *Strict Wilderness Reserves* shall denote:

A region under public control characterized by primitive conditions of flora, fauna, transportation and habitation wherein there is no provision for the passage of motorized transportation and all commercial developments are excluded.

There follow several articles dealing with the establishment of these parks and reserves.

The brief history of this convention takes us back to Resolution XXXVIII of the Eighth International Conference of American States, at Lima, Peru, in December, 1938, which provides for the establishment by the Pan American Union of a Committee of Experts, to study the problems of nature protection and wildlife preservation in the American Republics, and to formulate a Draft Convention for the preservation of the flora and fauna in the Western Hemisphere.

The Governing Board of the Pan American Union, in accordance with this resolution, called a meeting of the Committee of Experts for May, 1940, in the city of Washington.

The following countries were represented on this committee: Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, the Dominican Republic, Ecuador, Haiti, Mexico, Panama, Paraguay, Peru, the United States, Uruguay and Venezuela.

The committee held meetings from May 13 to 16 inclusive, at which it carefully considered material assembled in answer to a questionnaire sent out by the Pan American Union, and in accordance with this and with other information available prepared a draft of a convention which covers the important basic requirements for nature protection and wildlife preservation on a broad international basis for the American Republics. The draft of this convention received the unanimous approval of the above-mentioned committee of experts.

On October 12, the day on which the convention was opened for signature at the Pan American Union, representatives of the following countries affixed their signatures: Cuba, Ecuador, El Salvador, the United States, Nicaragua, Peru, the Dominican Republic and Venezuela. Other countries have signified their intention of signing in the near future.

Science, art and literature have forged strong ties between the American Republics. This convention should add still another tie through its parks, reserves and monuments, which will help to bring about a common interest in great masterpieces of creation in the Americas.

The signing of the convention was hailed by the Minister of El Salvador, Dr. Hector David Castro, in the following words:

> In affixing their signatures to the Convention on Nature Protection and Wildlife Preservation in the American Republics, the representatives of the nations of the Western Hemisphere have to-day pledged their countries to adopt measures for the protection of useful, harmless and ornamental species of plant and animal life. They have thus given formal recognition of the fact that many such species know no national boundaries, and that true conservation of the gifts of nature should begin before these resources have been dissipated by thoughtless or selfish destruction.
>
> This action brings together and thus strengthens all the unselfish efforts of individuals and governments throughout the countries of the New World. I am highly gratified that in a world so occupied with questions of grave political and military consequence a body of independent nations thus voluntarily agree upon a program aimed only at the peaceful end of protecting the endowments of a bountiful nature.

The spiritual value of the "natural beauty" that we hope to preserve for future generations in these great New World Continents can be most perfectly described in the following words of G. M. Trevelyan:

> By the side of religion, by the side of science, by the side of poetry and art, stands natural beauty, not as a rival to these, but as the common inspirer and nourisher of them all, and with a secret of her own besides. . . . It alone makes a common appeal to the sectaries of all our

religious and scientific creeds, to the lovers of all our different schools of poetry and art, ancient and modern, and to many more besides these. It is the highest common denominator in the spiritual life of to-day.

Let us hope that all the American Republics will sign, ratify and pass enabling laws to get the greatest benefit from this International Convention as soon as possible. We also hope that our Government, which stands first in conservation measures in the Americas, will lead the way by being the first to ratify.

HAROLD J. COOLIDGE, JR.,
*Chairman, Pan American Committee of the American Committee for International Wildlife Protection*
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# SPECIAL ARTICLES

## UPTAKE OF RADIOACTIVE PHOSPHORUS BY NUCLEI OF LIVER AND TUMORS

MICE carrying 10- to 15-day lymphoma[1] transplants were given 0.1 cc of isotonic $Na_2HPO_4$ containing 6–10 microcuries of $P_{32}$ by intravenous injection. At intervals afterwards the livers were cleared of blood by perfusion with saline, immersed in ice cold 5 per cent. citric acid for one-half hour, and the nuclei isolated by centrifugation of the pulped tissues. Tumors were removed from the same animals and similarly treated to obtain nuclei. Haemacytometer counts were made on all samples of nuclei, and contamination by fragments of cytoplasm was found to be negligible.

Fig. 1 shows the microcuries of $P_{32}$ per $cm^3$ packed

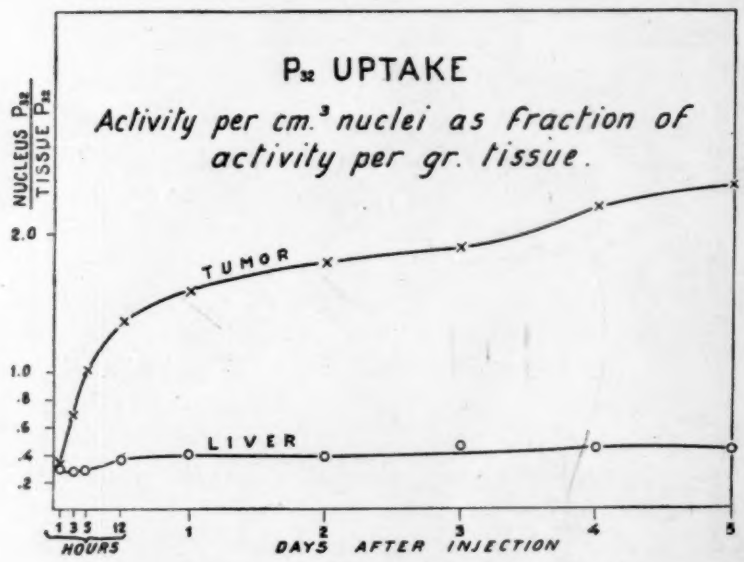


FIG. 1.

nuclei as a fraction of the $P_{32}$ activity per gram wet weight of whole tissue plotted against time after injection. Whereas the fraction of the liver $P_{32}$ bound by the nuclei remains constantly at .3–.4, the relative concentration in the tumor nuclei rises to more than twice that of the tumor tissue. Similar results have been obtained with sarcoma 180 in the mouse.

Isolated nuclei suspended in isotonic $Na_2HPO_4$ containing $P_{32}$ take up only one tenth the *in vivo* nuclear activity, and most of the *in vitro* activity can be shown to be adsorbed phosphate. Nuclei from liver slices shaken at room temperature in isotonic $Na_2HPO_4$ have less than one hundredth of the *in vivo* concentration of $P_{32}$. The uptake of $P_{32}$ can not therefore be attributed to simple chemical exchange.

After extraction with alcohol-ether and trichloracetic acid 60 to 70 per cent. of the $P_{32}$ of the liver nuclei is in the residue (nucleoprotein) and 70 to 95 per cent. of the $P_{32}$ of the tumor nuclei is in the same fraction at all intervals from one hour to five days after injection.[2] The data indicate that $P_{32}$ may be built into the nucleoprotein directly from the inorganic phosphate or that the rate of turnover in the more labile forms of organic phosphate is very rapid. Since the metabolic rate is lower in the rat than in the mouse, it is expected on the latter hypothesis that for comparable tissues (*e.g.*, liver) the relative $P_{32}$ concentration in the nuclei of the rat will be lower than for the mouse. From one-half hour to two days after injection of $P_{32}$ into 150-gram rats, the concentration in the liver nuclei is approximately 0.1 per cent. of the injected dose. The second alternative, therefore, seems the more probable.

To determine whether the greater concentration of $P_{32}$ by tumor nuclei is characteristic of the tumor *per se* or is to be attributed to mitotic activity, three 150-gram rats were partially hepatectomized and given $P_{32}$ intravenously 36 hours later. Three normal rats of the same weight, and three rats carrying bilateral carcinoma 256 implants were injected at the same time. Two days later livers and tumors were removed. The ratios of nuclear $P_{32}$ to tissue $P_{32}$ were .345, 1.02 and 1.08 for nuclei from normal liver, regenerating liver and tumor, respectively. With rats injected four days after partial hepatectomy and nuclei removed three days after $P_{32}$ injection, the ratios for nuclei from normal and hepatectomized animals were .28 and .32, respectively. Very few of these nuclei were found in mitosis, while of the liver nuclei removed in the first experiment 3.7 per cent. were in anaphase or metaphase and a much larger per cent. in prophase. The

[1] J. H. Lawrence and Gardner, *Am. Jour. Cancer*, 33: 112–119, 1938.

[2] The data are insufficient as yet for determining whether the difference in nucleoprotein $P_{32}$ of tumor and liver nuclei is significant. (71, 67, 64, 68, 53, 72 per cent. in liver nuclei at one hour, 1, 2, 3, 4, 7 days after injection and 98, 95, 94, 70 per cent. in lymphoma nuclei at 1, 3, 5, 7 days.) Preliminary data show no difference in nucleoprotein $P_{32}$ of rat liver and carcinoma nuclei.

greater $P_{32}$ uptake by tumor nuclei should therefore be attributed to mitotic activity.

There are $14.8 \times 10^{-10}$ mg P/liver nucleus and $12.8 \times 10^{-10}$ mg P/tumor nucleus. From the nuclear phosphorus composition and the nuclear $P_{32}$ content at 48 hours, the specific activity of tumor nuclei is found to be more than four times that of liver nuclei. Calculating from the daily $P_{31}$ retention[3] and the per cent. $P_{32}$ uptake, each nucleus will incorporate a quantity of $P_{31}$ equal to 8.9 per cent. of its $P_{31}$ content in five hours. It will thus take 56 hours for the nucleus to synthesize a quantity of $P_{31}$ equal to the amount it originally contained. This should be the time required to synthesize a new nucleus. This value agrees approximately with the observed rate of growth of the tumor which doubles in size in about two days at this phase of its growth curve.[4] It is interesting, though it may be purely a coincidence, that approximately the same time is obtained for the duration of the mitotic cycle in root tips by analysis of effects of x-rays and neutrons.[5]

A detailed account of these experiments will be presented elsewhere.

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## MODE OF ACTION OF ESTROGENS ON THE MAMMARY GLAND

FOLLOWING the demonstration by Lyons and Pencharz[1] in 1936 of the failure of estrogenic hormone to produce growth of the mammary glands of hypophysectomized guinea pigs, a sisable literature has appeared in confirmation of this work, which has been extended to include the rat, mouse, cat, rabbit and ground squirrel.[2] These observations emphasized the importance of the pituitary to the mammary gland and gave rise to the theory that injected estrogens exert their effects through the mediation of the pituitary, which was postulated to produce a specific mammogenic hormone.[3]

The specificity of the relationship between the pituitary and mammary growth has, however, been called into serious question by the demonstration[4] that in intact rats which were restricted to a diet comparable to that consumed by hypophysectomized litter-mates, the glands likewise failed to respond to administered estrogen. It has been shown,[5] further, that when hypophysectomized rats were treated with growth complex, growth of the mammary gland could be elicited by estradiol benzoate, and that the degree of stimulation could be correlated with the weight gain of the animals.

Recent experiments permit of a new approach to the problem of the mode of action of estrogenic substances on the mammary gland. By the direct application of the hormone to the nipple area it is possible to obtain a local effect on the nipple and mammary gland. In this manner one can observe the effects of the test substance in the intact animal, thereby obviating the complication of nutritional disturbances produced by hypophysectomy.

Immature male rhesus monkeys were used. The left nipple of each animal was painted daily with a solution of estrone in 95 per cent. alcohol, 0.05 mgm per cc. To the right nipple alcohol alone was similarly applied. Two animals were so treated for a period of 75 days. The entire glands were then removed. A third animal was treated in this manner for 50 days, and the breasts were removed 105 days later. The mammary glands were then fixed, dissected, stained and cleared, and studied as whole mounts.

In all cases the left mammary gland was distinctly larger and more developed than the right one (see Fig. 1). This difference in size exceeded, in each instance, the minor variations between right and left glands occasionally encountered in a study of more than 200 pairs of control monkey mammaries, including the breasts of 30 males.


FIG. 1. Right and left mammary glands of prepubertal male monkey after daily application of alcoholic solution of estrone to left nipple for 75 days. Silhouette tracings from photographs of actual specimens.

These observations are regarded as evidence for the direct action of percutaneously administered estrogen on the mammary gland. While not controverting the possible existence of pituitary mammogenic hormones,

[3] L. W. Tuttle, personal communication.
[4] Growth curves obtained from I. L. Chaikoff and H. B. Jones, unpublished.
[5] A. Marshak, *Proc. Nat. Acad. Sci.*, 25: 502–510, 1939.
[6] Fellow of the John Simon Guggenheim Memorial Foundation.
[1] W. R. Lyons and R. I. Pencharz, *Proc. Soc. Exp. Biol. and Med.*, 33: 589, 1936.
[2] E. T. Gomez and C. W. Turner, *Mo. Agr. Exp. Sta. Res. Bul.* 259, 1937.
[3] A. A. Lewis and C. W. Turner, *Mo. Agr. Exp. Sta. Res. Bul.* 310, 1939.
[4] E. B. Astwood, C. F. Geschickter and E. O. Rausch, *Am. Jour. Anat.*, 61: 373, 1937.
[5] I. T. Nathanson, D. T. Shaw and C. C. Franseen, *Proc. Soc. Exp. Biol. and Med.*, 42: 652, 1939.

or even the possibility of estrogenic stimulation of the production of mammogenic hormones by the pituitary, the present experiments offer no support for the view that administered estrogens necessarily stimulate mammary growth through the mediation of the pituitary. For if such were the case, a similar growth response would be expected in both glands, rather than the local, unilateral effect observed.

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## THE CONTROL OF PROTOPLASMIC STREAMING

PROTOPLASMIC streaming owes its existence to a motive force the magnitude of which has heretofore not been measured. In order that this might be done the technique here described has been developed.

The slime mold, *Physarum polycephalum,* served as material. Protoplasmic streaming in slime molds is extraordinarily active and exhibits a rhythmic reversal in direction of flow.

Small bits of plasmodia placed on cover-glasses coated with agar soon spread into thin sheets, which later develop protoplasmic strands. Among such cultures there are forms which can be changed so that there are two protoplasmic bodies connected by a single strand. A plasmodium thus shaped is inverted over a chamber which is divided into two compartments (A and B, Fig. 1) by an agar block (C, Fig. 1).

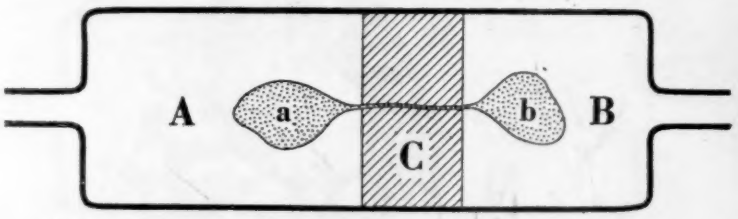


FIG. 1. Schematic representation of the chamber.

The construction is such that the two compartments may be kept airtight without the wall separating them blocking protoplasmic flow in the connecting strand. One of the two compartments is kept at constant atmospheric pressure, whereas the pressure in the other compartment is under control.

When there is no pressure difference between the two compartments, the shuttle movement of the protoplasm goes on normally, causing a corresponding change in the volume of the two protoplasmic masses (A and B, Fig. 1). When, however, a difference in air pressure is established between the two compartments, the movement of the protoplasm in the connecting strand is strikingly affected. If a slightly lower pressure (weak vacuum) is applied to one of the compartments, the flow of the protoplasm in the connecting strand into that compartment is accelerated. When a slightly higher pressure is applied to the same compartment, the flow of the protoplasm along the connecting strand into that compartment is retarded. If the pressure applied is stronger than the motive force developed in the plasmodium, then the forward-moving protoplasm is forced backwards. The direction and velocity of the protoplasmic movement in the connecting strand can thus be accurately controlled. Artificial control of protoplasmic streaming in this manner does not cause any observable damage. Flow continues normally after the applied pressure is released.

By this method it is possible to ascertain the precise degree of pressure necessary to hold the protoplasm at a standstill. The pressure at this point, which is regarded as equal in absolute value to the motive force responsible for the protoplasmic streaming, may be termed the balance-pressure. The range of the balance-pressure is usually between $\pm$ 20 cm of water. The maximum absolute value thus far encountered is 28 cm of water. So sensitive is the movement of the protoplasm that the slightest deviation (less than 0.2 cm of water) from the point of balance-pressure will induce movement in an 8 mm connecting strand.

As the motive force changes spontaneously, the balance-pressure must be adjusted accordingly, if the protoplasm is to be kept immobile. In order to determine in what manner and to what extent the motive force changes in relation to time, the instantaneous values of the balance-pressures (*i.e.,* the values taken at any given instant) are recorded at five-second intervals. By plotting a series of these values as ordinates against time as abscissas, undulating curves are obtained which faithfully portray the distinguishing features of the changes which the motive force undergoes during the rhythmic succession of vital processes. The graphs thus obtained give a complete view of the rhythm in protoplasmic activity. All characteristics of rhythm such as wave form, frequency, polarity and amplitude are portrayed by the graphical representation.

The study of many examples of wave trains mapped in this way leads to the conclusion that the characteristic change in amplitude and in form of wave is, in all probability, due to the interference of different rhythms. This concept necessarily implies the co-existence, in one and the same plasmodium, of different frequencies of the mechanism responsible for the motive force. In other words, a plasmodium is a polyrhythmic system.

In this brief note I am not in a position to go into further details of description and discussion of my experiments, except to say that in addition to an analysis of protoplasmic rhythm the method here touched upon is a means for attacking such problems as that of the relative influence of motive force and viscosity in protoplasmic flow. The procedure outlined above also suggests a new method for measuring protoplasmic viscosity by applying the principle of

the capillary viscometer which so far has been used only for non-living substances.

My special appreciation is due to Professor William Seifriz for his unfailing interest and critical supervision. This investigation was aided by a grant from Mrs. Curtin Winsor, to whom I wish to express my most sincere thanks.

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# SCIENTIFIC APPARATUS AND LABORATORY METHODS

## A SIMPLE METHOD OF MOUNTING SMALL EXHIBIT SPECIMENS OF MAMMALS AND BIRDS

AT regular intervals most scientists are confronted with the problem of presenting their work graphically to boards, patrons or laity. Biologists and medical researchers frequently must prepare taxidermic specimens used in their studies for such exhibits or for permanent museum record. Because an expense account seldom envisages the preparation of these demonstrations, professional assistance can not be readily procured.

It is for the above reasons that I believe my simple method of mounting small mammals is worth placing on record. This technique was first applied to mouse specimens exhibited at the Harvard Tercentenary in 1936, and more recently it has been employed on rats for the museum collections of the Wistar Institute, where they will be pointed out upon request. There is no reason why this method can not be readily extended with modifications to small birds and mammals generally.

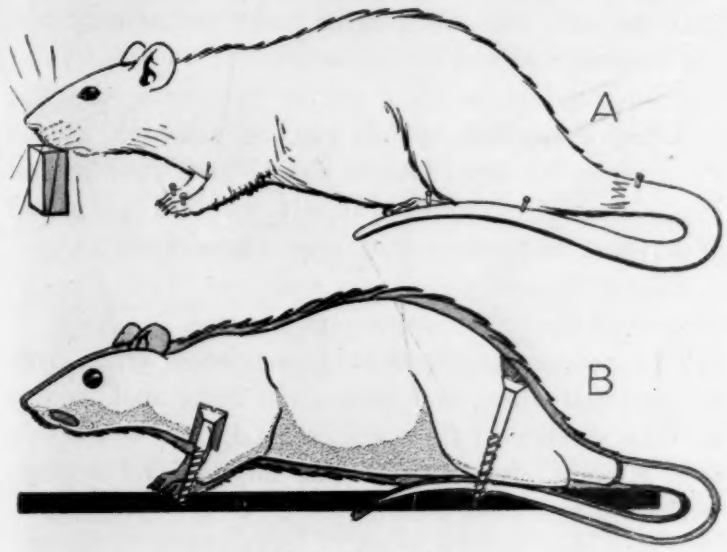
For the sake of simplicity I shall here describe the method as applied to the rat. First, kill the rat with a lethal dose of ether, chloroform or by some other method that will not harm the anatomy.

Inject 10 cc of 40 per cent. formaldehyde into the thoracic cavity and another 10 cc into the abdominal cavity, massaging the animal to distribute the injection fluid within the body cavities. Inject small amounts into the legs and subcutaneously over the body.

Within 15 minutes to half an hour subsequent to this injection the body will stiffen. When fairly rigid, place the rat upon a small temporary base-block of wood in the position desired for the finished specimen. Brad the rat's tail to the block. Then brad the four feet to their proper positions bending the body into the pose desired. The hips may be prevented from moving laterally by hammering several 7-penny nails into the block adjacent to the hips. The head may be held up by resting the teeth on a block of proper dimensions. See Fig. A.

When the animal is in the position desired, allow it to stand an hour or so until it has completely hardened.

Invert the specimen and wash it thoroughly under a faucet so water will wet the whole outer surface of the skin. Place the inverted specimen, block and all, into a jar of formalin and allow it to stand 24 hours. The previous washing removes all air caught in the fur that might prevent areas of the skin from coming in contact with formalin.




FIGS. A and B.

After the specimen has cured 24 hours in formalin, wash under the faucet for a few minutes to remove all traces of formalin, which will attack the skin of the operator's hands, unless they are otherwise protected.

Lay the specimen on its back, and with a sharp razor blade cut the skin along the mid-ventral line from throat to genitals. Cross-slit between the two wrists and also between the two ankles. Now skin the animal. Wash from time to time to remove formalin from the interior. Sever the feet, leaving them attached to the skin of the legs. By first rolling the tail vigorously, the skin of this appendage may be readily slipped off. If difficulty is here encountered, a slit may be made along the ventral surface of the tail.

The detached skin, which tends to retain the shape of the posed specimen, is put back into the jar of formalin to harden further.

The body is then placed in its normal position in a small box to support the body mold which is cast from hide glue, plaster or a recently patented substance known as Plastico which has an agar base. When the mold has hardened, slit it longitudinally and remove the body. Cast a duplicate body in the mold with plaster or wax, preferably the former. Any projections produced in casting the body may be cut away with a knife and any depressions that may occur can be filled with Plasticine. The tail skin

may be filled with plaster, wax or fine lead shot. Arrange a permanent black wooden mounting and adjust two screws to run through the plaster body sagitally so as to hold the finished specimen in the position desired. See Fig. B.

Set artificial eyes (beads or glass pin heads) in their depressions on the head of the plaster body. Wash the skin in water. Dry it with paper towels. Slip the skin over the plaster body and sew up the one longitudinal and two cross-slits.

Brad the feet to their proper positions. In life such regions as ears, eyelids and toes are pink, due to the presence of subcutaneous blood vessel distribution. These areas may be tinted lightly with red ink mixed with water to produce the appropriate shade.

Adjust eyelids, nose, ears and feet from time to time until the finished specimen hardens.

Two great advantages of this method aside from its simplicity are, first, that each individual retains its individuality of form and, second, that each specimen may be caused to assume any one of a great variety of possible poses.

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## A MICROPHOTOGRAPHIC CAMERA

IN the May 24 issue of SCIENCE[1] Abrahamson described "An Inexpensive Microphotographic Camera." For those interested in making an occasional photomicrograph a very simple method was described and illustrated by Turrell.[2]

The microscope is focused and a cheap vest pocket kodak, fitted with a yellow filter, is placed on the eyepiece, being kept in position by its own weight. Exposure is made with a cable release. If a focusing camera is used the focus should be set for infinity and the lens diaphragm should be wide open. When using a 10× ocular, the image circle does not fill the entire negative area, but it can be enlarged.

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## AUTOMATIC MERCURY VALVE

THIS simple valve arrangement will prevent the forcing or accidental spilling of mercury from an open tube, yet offers negligible resistance to the flow or oscillation of the mercury.

The stainless steel ball "B" and the constriction "A" (ground to a 45° angle) will form a valve that will stop the falling (Fig. 1) or rising (Fig. 2) mercury column "C" at "A."

With a valve (as shown in Fig. 1) located on the citrate side of a mercury manometer such as is used for direct blood pressure recording, it is impossible for excessive pressure to expel the mercury.

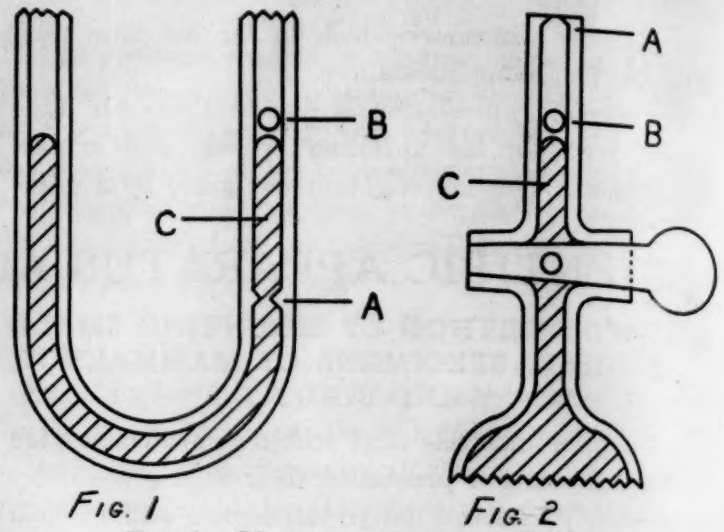


FIG. 1 FIG. 2

FIG. 1. Mercury manometer (Pyrex).
FIG. 2. Air sampling tube (Pyrex).

Air sampling tubes equipped as in Fig. 2 will permit rapid positive evacuation without the usual overflow of mercury.

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[1] SCIENCE, 91: 509, 1940.
[2] F. M. Turrell, Trans. Am. Micros. Soc., July, 1933, 267.